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PROLONGED ENDOTRACHEAL INTUBATION

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PROLONGED ENDOTRACHEAL INTUBATION

A Clinical Investigation
with Special Reference to its Consequences
for the Larynx and Trachea and to its Place as an Alternative to
Intubation through a Tracheostomy

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av

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By

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1969 - SUPPLEMENTUM XXXIII

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NOTATION AND DEFINITIONS

Infants:
$<$ 1 year old.

Children:
1–15 years old.

Adults:
$>$ 15 years old.

Case nos. 1–332:
Adult patients in follow-up series and post mortem series in chronological order.

Case nos. C1–C55:
Infants and children in follow-up series and post mortem series in chronological order.

Prolonged endotracheal intubation:
Endotracheal intubation for longer than 24 hrs.

Period of intubation:
The primary period of endotracheal intubation + periods of reintubation if these occurred within 1 week after the primary period.

Period of healing:
The length of time from the end of the period of endotracheal intubation up to the time when, on inspection, the laryngeal status was considered to have returned to normal.

Acute damage:
Damage observed within 1 week after the period of endotracheal intubation.

Postintubation:
Occurring after the end of the period of endotracheal intubation.

Late damage:
Damage persisting at the follow-up examination.

Primary tracheostomy:
Tracheostomy without preceding prolonged endotracheal intubation.

Secondary tracheostomy:
Tracheostomy immediately after prolonged endotracheal intubation.

IPPV:
Intermittent positive pressure ventilation.

PVC:
Polyvinyl chloride.

I.d.:
Internal diameter.

E.d.:
External diameter.

In calculating the percentage proportion for different groups in a series, this was done on the total number of patients for whom the information in question was available. The patients who came under the heading "not recorded" or "not examined" were thus excluded from the total number in these calculations.

INTRODUCTION AND AIM OF THE INVESTIGATION

Intensive care has rapidly become of increasing importance in hospital treatment. The chief task in this form of medical care is to supervise the vital functions of the severely ill patient and when necessary to give temporary aid to or take over completely by mechanical devices one or more of these functions. In this respect, artificial ventilation by means of a respirator is probably the most common measure. The most commonly used respirator in Sweden today was designed by Engström in 1951 to deliver a predetermined ventilatory volume.

In volume controlled intermittent positive pressure ventilation (IPPV) the respirator has usually been connected to the patient's upper respiratory tract through a tracheostoma via a tracheal cannula. During the last decade, however, many intensive care units have chosen, in an increasing number of cases, to use an indwelling orotracheal or nasotracheal tube as an alternative to the above technique, even during longer periods of respirator treatment in conscious patients. Prolonged endotracheal intubation has also been used to produce a free airway in unconscious patients breathing spontaneously, in patients with upper airway obstructions due to allergy, infection or trauma and also to facilitate repeated aspiration of bronchial secretions. In many earlier investigations concerning the risk of complications from endotracheal intubation, it has been claimed that an intubation period exceeding 24 hours (Sieker and Hickam, 1956, Leegaard, 1960, Bergström, 1962) greatly increases the risk of laryngeal complications. The time factor seems to have attracted more attention than some other important factors such as the material, diameter and shape of the tube, the degree of laryngeal motor activity during the period of intubation and the humidity of the inspired or insufflated air.

Recent investigations (Brandstater, 1962, Allen and Steven, 1965, Jackson Rees and Owen-Thomas, 1966, among others) indicate that if due consideration is taken of these factors a laryngeal tube introduced through the mouth or nose can be left in position for considerably longer than 24 hours without noteworthily increasing the risk of serious laryngeal complications; a risk which in any case must be weighed against the risks associated with tracheostomy.

Possibilities of evaluating, in the acute stage, the risk of late complications would seem desirable. If this could be done, a period of prolonged endotracheal intubation could possibly be interrupted before the occurrence of damage that might give late complications, and could be replaced by tracheostomy.

During the last four years the use of prolonged endotracheal intubation as an alternative to tracheostomy has increased greatly at the departments of intensive care of the University Hospital in Uppsala (Tables 1 and 2), and this method has been employed mainly for periods of respirator therapy. The question of the justification of prolonged endotracheal intubation is still controversial and this was considered to motivate a systematic study of patients, both adults and infants and children, treated with this technique.

The aims of this investigation were to study:

1. Complications during the period of endotracheal intubation.
2. Complications immediately after the period of endotracheal intubation.
   Especial interest was paid to the following problems:
   Localization and type of mucosal reaction in the larynx and trachea immediately following endotracheal intubation of more than 24 hours.
   The extent of acute mucosal lesions and, by means of certain criteria, the healing course and the risk of permanent damage.
   The extent and healing course of mucosal lesions caused by an endotracheal tube in relation to various data concerning the patient, the duration of intubation, the material, diameter and shape of the tube and the degree of laryngeal motor activity during the period of intubation.
3. Late complications.
4. The possibility of modifying the technique, to reduce the incidence of complications.

TABLE 1.

Patients treated with endotracheal intubation or tracheostomy at the University Hospital, Uppsala. (Intubation for general anaesthesia only not included.) Figures in brackets give the numbers of patients treated by IPPV.
The figures under the heading "endotracheal tube" represent patients who were endotracheally intubated only. Those under the heading "tracheostomy" also include patients who were initially endotracheally intubated for a certain period and then tracheostomized.

Department	Endotracheal tube	Tracheostomy	No. of patients
	1960–1963		
Thoracic intensive care unit[1]	0 (0)	269 (269)	269 (269)
General intensive care unit[1]	111 (57)	209 (172)	320 (229)
No. of patients	111 (57)	478 (441)	589 (498)
	1964–1967		
Thoracic intensive care unit	359 (358)	241 (240)	600 (598)
General intensive care unit	548 (429)	263 (220)	811 (649)
No. of patients	907 (787)	504 (460)	1411(1247)

[1]) The units described by HOLMDAHL (1962).

In order to evaluate the use of prolonged endotracheal intubation as an alternative to tracheostomy, the complications resulting from the latter procedure as recorded in the literature are also surveyed.

TABLE 2.

Patients endotracheally intubated >24 hours at the University Hospital, Uppsala 1964–1967.

Age Groups (Years)	Surviving patients	Deaths[1])	No. of patients
Thoracic intensive care unit			
0– 2	5	5	10
3– 5	4	2	6
6–15	17	3	20
>16	321	43	364
No. of patients	347	53	400
General intensive care unit			
0– 2	16	20	36
3– 5	4	1	5
6–15	5		5
>16	141	106	247
No. of patients	166	127	293

[1]) Deaths due to primary disease.

Chapter I

SURVEY OF THE LITERATURE CONCERNING INTUBATION AND TRACHEOSTOMY

A. *Endotracheal intubation*

1. *History*

In 1880, William MacEwen published "Clinical observations on introduction of tracheal tubes by the mouth instead of performing tracheostomy or laryngotomy". This is the first time that prolonged endotracheal intubation is encountered in the literature; one of MacEwen's patients had a tube *in situ* for 35 hours and another for 36 hours. Many of this investigator's perspicacious observations and far-sighted conclusions have since proved to be correct. He realised the possibility of using endotracheal intubation to obtain a free airway, to administer anaesthetics and to prevent aspiration of blood at operations in the face and mouth. O'Dwyer (1887) reported encouraging results of intubation of the larynx with short metal tubes in 50 cases of diphtheria, and especially in the United States this method was widely used. Later (1894) he pointed out the applicability of the method in chronic laryngeal stenosis and in decannulation difficulties. In 1910 Elsberg demonstrated the value of translaryngeal intubation in anaesthesia during thoracic surgical operations, and subsequently the intubation method in anaesthesia began to gain ground, although it was long regarded with mistrust. Magill and Rowbotham further developed methods for endotracheal intubation in 1917–21 (cf. Evans and Gray, 1965), and investigations on the frequency of complications in endotracheal intubation in connection with anaesthesia have shown that serious injuries occur very rarely (Jackson, 1913, Donnelly *et al.*, 1948, Arner and Diamant, 1951, and others).

Prolonged endotracheal intubation in adults was reported in isolated cases during the 1940's (Gillespie, 1942, Foregger, 1946, Briggs, 1950, Urry, 1951). In Scandinavia this method began to be used more frequently in the 1950's in the treatment of patients with drug poisoning (Nilsson, 1951, Dam and Zwergius, 1952, Clemmesen and Nilsson, 1961, Bergström, 1962), and during the 1960's it was used in some clinics for postoperative respirator therapy in patients who had undergone open-heart surgery (Dammann, 1965, Holmdahl and Westerholm, 1965), after other major operations and in a number of conditions with "ventilatory insufficiency" or "relative hypoventilation" (Holmdahl and Westerholm, 1965, Tonkin and Harrison, 1966, Holmdahl and Lindholm, 1967, Pilcher, 1967, Weg, 1967, Lindholm, 1968).

Brandstater (1962) reported that the method was used with good results in the treatment of 12 children as an alternative to tracheostomy. This report

was followed by several publications in which the authors described their experiences of prolonged intubation in children and recommended technical improvements (Allen and Steven, 1965, McDonald and Stocks, 1965, Fearon *et al.*, 1966, Jackson Rees and Owen-Thomas, 1966, Suutarinen *et al.*, 1966, Holmdahl and Lindholm, 1967, Owen-Thomas, 1967, Roth *et al.*, 1967, Striker *et al.*, 1967, Abbott, 1968, Feychting and Settergren, 1968, Hatch, 1968, Stocks, 1968, Tunstall *et al.*, 1968, VerMeulen and Birck, 1968).

2. *Complications of prolonged endotracheal intubation*

The problems of prolonged endotracheal intubation as found in the literature will be surveyed under the following headings:

a. Complications of the intubation technique.
b. Complications during the period of endotracheal intubation.
c. Early complications following the period of prolonged endotracheal intubation.
d. Late complications following prolonged endotracheal intubation.

ad a. The intubation procedure itself does not, in the majority of cases, give rise to serious complications if it is performed by an experienced anaesthesiologist. It is true that an endotracheal tube has been reported to give rise to a false pathway during its introduction (Haxholdt, 1954, Abbott, 1968), but usually the damage is limited to minor mucosal lesions in the mouth or throat, and dental injuries. In the case of technical difficulties during this procedure, however, the laryngeal lesions which sometimes occur after prolonged intubation may be more extensive (Tonkin and Harrison, 1966).

ad b. An obstructed airway due to dried or inspissated secretions in the endotracheal tube has sometimes caused serious problems, especially when fine-calibre tubes have been used (Fearon *et al.*, 1966, Aberdeen and Glover, 1967, Holmdahl and Lindholm, 1967, Striker *et al.*, 1967, Abbott, 1968). With adequate humidification of the inspired or insufflated air, however, the risk of this complication seems to have diminished considerably, which has been pointed out by several authors (Brandstater, 1962, McDonald and Stocks, 1965, Jackson Rees and Owen-Thomas, 1966, Atherstone and Ryder, 1967). Aspiration of the endotracheal tube, as well as accidental extubation with a fatal outcome has been described (Aberdeen and Glover, 1967, Striker *et al.*, 1967), and 5 cases of "swallowed endotracheal tube" in connection with suctioning and ventilation of newborns, all without further complications, were reported by Dickson and Fraser (1967). The risk of these above complications is probably very small if the nasotracheal tube introduced by Jackson Rees and Owen-Thomas (1966) is used.

Inadequate ventilation of the left lung can occur if the tube happens to

be inserted too far or to slide down into the right primary bronchus during the period of intubation.

Aspiration of the bronchial secretions by suctioning is usually considered to be more difficult through an endotracheal tube than through a tracheostoma. No information as to whether this circumstance more often gives rise to atelectasis or bronchopneumonia during endotracheal intubation than in cases of tracheostomy could be found in the literature.

ad c. If endotracheal intubation has been performed because of upper airway obstruction (e.g. acute laryngotracheitis), it is obvious that reintubation or tracheostomy may be necessary (Allen and Steven, 1965) after removal of the endotracheal tube. Following prolonged endotracheal intubation in cases where primarily the laryngeal status was normal, laryngeal oedema has, however, occurred on some occasions after extubation (Dam and Zwergius, 1952, McDonald and Stocks, 1965, Tonkin and Harrison, 1966, Aberdeen and Glover, 1967, Markham *et al.*, 1967). This condition has also been described after short-term intubation anaesthesia (Crispell and Hampton, 1950, Baron and Kohlmoos, 1951, Haines and Powell, 1955). It is evident from the literature that this complication mainly affects children and sometimes indicates tracheostomy (Table 3). The histologic structure of the subglottic mucosa and also the fact that "the cricoid cartilage is the only complete cartilaginous ring in the trachea" are probably the most important factors for the development of acute subglottic stenosis (Holinger and Johnston, 1950). This has also been pointed out by other authors (Eckenhoff, 1951, Haines and Powell, 1955), and in cases where subglottic oedema has occurred it seems, as a rule, that tubes with too large an outer diameter in relation to the lumen of the larynx have been used (Haines and Powell, 1955, Way and Sooy, 1965, Weg, 1967).

Ulceration on the alae nasi has been reported after prolonged nasotracheal intubation (Owen-Thomas, 1967) but ulceration and necrosis in the larynx are considerably more common (Bergström *et al.*, 1962, Tonkin and Harrison, 1966, Holmdahl and Lindholm, 1967, Hedden *et al.*, 1969). Superficial ulcerations surrounded by oedema have been observed, further, in the trachea where the inflated cuff of the endotracheal tube has been located (Lindholm, 1968).

An inflammatory reaction of the pseudomembranous type within the larynx and trachea has been described after intubation anaesthesia (Muir and Straton, 1954, Stein *et al.*, 1960, Lu *et al.*, 1961) and with prolonged intubation some cases have been reported with "laryngeal slough" (Tonkin and Harrison, 1966), "purulent membranes" (Dam and Zwergius, 1952) and "necrotizing tracheitis" (Fearon *et al.*, 1966). Further, Jackson Rees and Owen-Thomas (1966), who have considerable experience of very long periods of endotracheal intubation, have drawn attention to the risk of subglottic membrane 19–24 hours after extubation.

ad d. The most feared of the late complications of prolonged endotracheal intubation is subglottic cicatricial stenosis. This condition is most common in children and is reported to occur with very varying frequencies in different clinics.

In adults, Minnigerode (1968) and Bryce *et al.* (1968) reported subglottic cicatricial stenosis after prolonged endotracheal intubation, while partial adhesion of the vocal cords was reported in 3 cases by Dam and Zwergius (1952) and immobilization of the arytenoids by a posterior band of fibrous tissue was described by Harrison and Tonkin (1967). Warner (1967) described, further, a case of "subglottic laryngeal band", which had probably been caused by prolonged intubation.

In children, several cases of subglottic cicatricial stenosis have been reported. No fewer than 6 children had "severe subglottic stenosis" and 1 child a "glottic web" out of 29 surviving patients in a series of Fearon *et al.* (1966). In an article by Striker *et al.* (1967) it is stated that out of a series comprising 80 children, 7 had subglottic stenosis, and the stenosis frequency was overrepresented in the group of children primarily intubated because of "upper airway obstruction". Out of 33 surviving children in a Swedish series, 8 were reported by Feychting and Settergren (1968) to have developed "subglottic stenosis of a rigid, narrow type". Reintubation was performed in 6 of these children and the endotracheal tube left in for about one week, after which it was removed permanently. The remaining 2 children were tracheostomized and subsequently developed serious subglottic stenosis. McDonald and Stocks (1965) recommended caution in prolonged endotracheal intubation of children with acute laryngotracheobronchitis, in view of the increased risk of cicatricial stenosis in this condition. Allen and Steven (1965) reported, however, only one "cicatricial stenosis" and one "glottic web" among 51 surviving infants and children, the majority of whom were intubated because of acute laryngotracheobronchitis. Jackson Rees and Owen-Thomas (1966) encountered this complication in 2 cases out of a series of 126 infants and children treated with prolonged endotracheal intubation, and in these 2 patients the intubation periods were extremely long (about 2 and 3 months). Markham *et al.* (1967) reported 2 cases of subglottic web formation and 3 cases of subglottic cicatricial narrowing among 74 surviving infants and children, and Hatch (1968) 3 cases of subglottic cicatrical narrowing among 57 surviving infants and children.

In Table 3, the frequencies of subglottic cicatricial stenosis given by 14 authors are presented. In two reports (Fearon *et al.*, 1966, Striker *et al.*, 1967) it is not stated whether all stenoses were of the fibrous type, but the figures have been included nevertheless. The frequency of fibrous stenosis in these series may therefore, in reality, be somewhat lower than is indicated by Table 3.

The cause of subglottic stenosis is with the greatest probability the occurrence of circular ischaemic pressure necrosis at the level of the cricoid due to the use of a tube which is too wide in relation to the lumen of the larynx (Allen and Steven, 1965, McDonald and Stocks, 1965, Holmdahl and

TABLE 3.

Acute respiratory obstruction leading to tracheostomy, and clinically significant fibrous subglottic stenosis, following prolonged endotracheal intubation in infants and children reported in the literature.

Authors and period of investigation	No. of patients treated with prolonged endotracheal intubation	No. of surviving patients	Range of intubation period in surviving patients (days)	No. of patients with acute respiratory obstruction leading to tracheostomy following extubation	No. of patients with fibrous subglottic stenosis causing functional impairment
BRANDSTATER 1959–1962...	12	9	3–49[1])		0 (0.0%)
ALLEN and STEVEN 1963–1964.....	61	51	1–"28 ; "[1]) (80% of the patients <14 days)	4 (7.8%)	1 (2.0%)
MCDONALD and STOCKS 1963–1964[2])	50	29	1–14 (25 pat. <7 days)	7(24.1%)	1 (3.4%)
FEARON *et al.* 1965–1966...	72	29	8 hrs–42 days[1])	7(24.1%)	6(20.8%)[3])
HOLMDAHL and LINDHOLM 1964–1966.....	32	21	1–21 (20 pat.<7 days)	5(23.8%)	1 (4.8%)
OWEN-THOMAS (1967)[4]).....		39	8 hrs–60 days (2/3 of the patients <7 days)		2 (5.1%)
ROTH *et al.* 1965–1966.....	29	25	1–8		1 (4.0%)
STRIKER *et al.* 1964–1966...	116	80	Not stated	3 (3.8%)	7 (8.8%)[3])
MARKHAM *et al.* 1965.....	156	74	1–43 (38 pat. <7 days)	5 (6.8%)	3 (4.1%)
ABBOTT 1964–1966[4]).....	83	30 (26 cases investigated)	1–17 (15 pat.<7 days)		2 (6.7%)
FEYCHTING and SETTERGREN (1968).....		33	Not stated	2 (6.1%)	2 (6.1%)
HATCH 1965–1967.....	134	57	1 hr–34 days[1]) (50 pat.<7 days)	5 (8.8%)	3 (5.3%)
TUNSTALL *et al.* (1968)[5])...	90	33	Mean duration of IPPV 73 hrs		0 (0.0%)
STOCKS 1963–1968[2]).....	first 60	146	Mean duration[1]): infants 5.6 children 5.4	6	2
	last 225		Mean duration[1]): infants 11.4 children 5.4	0	0
				(4.1%)	(1.4%)

[1]) Reported for the total no. of patients.
[2]) Seem partly to be the same series.
[3]) Not stated whether all stenoses were of the fibrous type.
[4]) Seem partly to be the same series.
[5]) Newborn infants only.

LINDHOLM, 1967). BRYCE *et al.* (1968) consider that the most important risk of damage lies in the inflated cuff of the endotracheal tube.

Isolated cases of ankylosis of the crico-arytenoid joint in adults have been reported as a result of damage by prolonged endotracheal intubation (MINNIGERODE, 1962, 1968, ROTH *et al.*, 1967).

Granuloma formation at the level of the vocal cords is more common in adults than in children. Several cases have been reported after intubation anaesthesia (Jackson, 1953, Epstein and Winston, 1957, among others). The frequency of this condition seems to be low, however, (Howland and Lewis, 1956). Jackson (1953) discussed the mechanism for the occurrence of these "contact ulcer granulomas" and stated: "granuloma is a secondary lesion due to frustration of healing regardless of the cause of primary trauma". Epstein and Winston (1957) summarized 55 cases reported in the literature, presented 10 cases of their own and treated the aetiology, pathogenesis, histology, prophylaxis and therapy in a review.

Several authors have described granuloma formations of the same kind after prolonged intubation (Nilsson, 1951, Dam and Zwergius, 1952, Bergström, 1962, Elbrønd, 1964, Harrison and Tonkin, 1965, Tonkin and Harrison, 1966), and Hawle (1966) reported a patient with multiple telangiectatic granulomas in the trachea after intubation for more than 24 hours.

Children are apparently affected more seldom by intubation granuloma. Striker *et al.* (1967), however, observed "subglottic granuloma" in 2 cases and "papilloma of the vocal cord" in 1 case of a series of 116 children, and Allen and Steven (1965) and Stocks (1968) stated that they had observed some granulomas that had regressed spontaneously.

The total complication frequency in prolonged endotracheal intubation of adults is difficult to determine, since it is seldom given in the literature.

In an analysis by Tonkin and Harrison (1966) of 166 patients who had been intubated for a mean period of 29.1 hours, 4.2% of acute laryngeal lesions were classified as "severe damage" and 13.3% as "moderate damage". None of these gave permanent disabilities, however.

In adults, post-intubation granulomas generally dominate among the complications. These have been reported in 0–8% and have not usually given rise to permanent disabilities (Nilsson, 1951, Bergström, 1962, Elbrønd, 1964, Kuner and Goldman, 1967, Weg, 1967, Hansen and Jørgensen, 1968). As mentioned previously, however, in some cases adult patients have sustained permanent damage (Dam and Zwergius, 1952, Harrison and Tonkin, 1967, Roth *et al.*, 1967, Minnigerode, 1962, 1968, Bryce *et al.*, 1968).

The total complication frequency in prolonged endotracheal intubation of infants and children has been given by Striker *et al.* (1967) as 22%, by Abbott (1968) as 61% and by Hatch (1968) as 29%. Stocks (1968) and Allen (1968) report considerably fewer complications in the hitherto largest series in which prolonged endotracheal intubation has been used (285 patients. and over 200 patients, respectively).

In children, the majority of complications have usually occurred during the period of intubation and have usually consisted of obstruction of the airway. The most important of the complications in children after the period of intubation have been presented in Table 3.

3. *Mortality*

Among publications of seven authors concerning altogether more than 400 adult patients treated with prolonged endotracheal intubation, I was unable to find any evidence of deaths occurring as a direct consequence of this form of treatment (Bergström, 1962, Tonkin and Harrison, 1966, Kuner and Goldman, 1967, Pilcher, 1967, Roth *et al.*, 1967, Weg, 1967, Hansen and Jørgensen, 1968).

In children, on the other hand, a number of authors have reported cases of death in this connection. Striker *et al.* (1967) reported 2 deaths in their series (116 patients), which had been caused directly by an obstructed airway in connection with prolonged endotracheal intubation (in 1 case due to dislocation of the tube and in 1 case due to aspiration of the tube) and Aberdeen and Glover (1967)[1]) stated that 5 out of 62 children had died as a direct result of complications during the intubation period (1 child because of a dislocated tube and 4 children because of "inspissated secretions" in the tube with obstruction as a result). Abbott (1968)[2]), reported 1 death (due to "obstruction of the tube") among 83 children and McDonald and Stocks (1965)[3]) and Fearon *et al.* (1966) each reported 1 death, out of a total of 122 infants and children where subglottic stenosis may have contributed to the fatal outcome. Other authors, who described altogether 631 cases, reported no mortality caused by prolonged endotracheal intubation (Brandstater, 1962, Allen and Steven, 1965, Jackson Rees and Owen-Thomas, 1966[2]), Suutarinen *et al.*, 1966, Holmdahl and Lindholm, 1967, Markham *et al.*, 1967, Roth *et al.*, 1967, Owen-Thomas, 1967[2]), VerMeulen and Birck, 1968).

Altogether 10 deaths had thus occurred among a total of between 1200 and 1300 children as a certain or probable complication of prolonged endotracheal intubation. The majority of the deaths (8 cases) occurred during the period of intubation as a result of an obstructed airway.

B. *Intubation through a tracheostomy*

1. *History*

Tracheostomy is a procedure which up to and in the early 1940's was carried out mainly on the indication of upper airway obstruction (Figi, 1934, Eve, 1943, Miller, 1948, Neffson, 1949, Quist-Hanssen, 1953). As early as in 1871, however, Trendelenburg pointed out the applicability of tracheostomy in inhalation anaesthesia and constructed the first tracheostomy tube with an inflatable cuff.

During the 1940's Galloway (1943) demonstrated the importance of tracheostomy in the care of poliomyelitis patients with respiratory insufficiency.

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[1]) This study seems to treat partly the same series as Hatch (1968).

[2]) These studies seem to treat partly the same series.

[3]) This study seems to treat partly the same series as Stocks (1968).

By this procedure the airway could be kept free by repeated suctioning of the bronchial tree, the dead space was diminished and the possibility was obtained of assisting or completely taking over the ventilation by means of a respirator. During the poliomyelitis epidemics in Scandinavia in 1950–1953, treatment according to these principles was often life-saving (SJÖBERG, 1956, SJÖBERG *et al.*, 1952, ENGSTRÖM, 1953, LASSEN, 1953, IBSEN, 1954).

Because of the good results thus achieved by IPPV, the indications for this form of treatment were extended, to include an increasing number of types of respiratory insufficiency regardless of their cause. For further details in this respect the reader is referred to the publication "Controlled ventilation in medical practice" (NORLANDER, BJÖRK, CRAFOORD, FRIBERG, HOLMDAHL, SWENSSON, WIDMAN, 1961). The development outlined above has resulted in a large increase in the frequency of tracheostomies during the last two decades (NELSON and BOWERS, 1957, MOLLARET *et al.*, 1962, WATTS, 1963, VON SCHULTHESS, 1964, JOHNSTON *et al.*, 1967).

2. *Complications of tracheostomy*

The problems of tracheostomy as found in the literature will be surveyed under the following headings:

a. Complications of the operative procedure.
b. Complications during the period of tracheostomy.
c. Early complications following the period of tracheostomy.
d. Late complications following tracheostomy.

ad a. Respiratory arrest, cardiac arrest and shock occurred not seldom during the "preanaesthesiological period". During later years these often fatal complications have been greatly reduced in number due to the rapid development of anaesthesiology (VON SCHULTHESS, 1964).

Technical complications during the operative procedure, in the form of damage to the cricoid cartilage and first tracheal ring (JACKSON, 1921, among others), oesophageal perforation (GLAS *et al.*, 1962, HEDDEN *et al.*, 1968) haemorrhage (NELSON *et al.*, 1957, among others) damage to the recurrent laryngeal nerve (WEBER, 1963) and air embolism (ASHERSON, 1958) have been reported.

The frequency of mediastinal emphysema and pneumothorax has varied considerably in different investigations, but on the average it seems to have been higher in children (QUIST-HANSSEN, 1953, TOREMALM, 1960). In the review by NELSON and BOWERS (1957) mediastinal emphysema and pneumothorax were reported in 6 and 7 cases, respectively, out of 310 tracheostomies, the majority of which were performed under local anaesthesia. GLAS *et al.* (1962) reported pneumothorax in 2 cases out of 80 such operations, bud did not mention mediastinal emphysema. QUIST-HANSSEN (1953), in a study of 468 patients who were tracheotomized because of acute laryngeal stenosis, noted

21 cases of emphysema and/or pneumothorax in connection with the tracheostomy. None of these authors stated whether postoperative chest X-ray had been performed routinely.

In children below 10 years of age, it is reported in the presentation by Toremalm (1960) of the tracheostomy series of nine authors that mediastinal emphysema occurred in 12–75% and pneumothorax in 6–25%. On the other hand, among the 25 tracheostomies on children below the age of 10 years reported by Toremalm himself, only one mediastinal emphysema and no pneumothorax occurred. Oliver *et al.* (1962) reported postoperative mediastinal emphysema and pneumothorax in 6.1% and 5.8%, respectively, in a statistical study of 294 "tracheotomy operations" performed on children below the age of 18 years. These authors, and also Neffson (1943), Forbes *et al.* (1947), and Aschan and Sandström (1960) demonstrated clearly that intubation during the operation diminished the risk of these complications. Aberdeen and Glover (1967) stated that among more than 200 tracheostomized children there had been no problems with mediastinal emphysema or pneumothorax. This was a series of thoracic surgical patients, however, and it can be assumed that in most cases the tracheostomies were performed when there was drainage of the chest.

The pathogenesis in the occurrence of mediastinal emphysema and pneumothorax was discussed as early as in 1882 by Champneys, who demonstrated that this complication was the result of "excessive inspiratory effort". Several authors (Neffson, 1943, Bergström and Diamant, 1960, Oliver *et al.*, 1962) have since discussed the mechanism for the occurrence of this complication. These conditions occur in patients with the pretracheal space open and an obstructed airway in association with forced inspiration. In this situation, owing to the large negative pressure in the thorax, air is drawn via the pretracheal space into the mediastinum and sometimes further into the pleural space. This has been demonstrated experimentally by Forbes *et al.* (1947.) In the case of forced expiration in association with a blocked cannula and with the skin fitting tightly around the cannula, an emphysema can develop, which is usually first distributed subcutaneously (Holinger and Johnston, 1960) and may be accompanied by pneumothorax. Lesions on the pleural cupulae and ruptures of alveolar sacs are also considered to be a possible cause of pneumothorax. The first of the mechanisms mentioned above explains the high frequency of this kind of complication when the operation has been performed under local anaesthesia or under inhalation anaesthesia without intubation on the indication of upper airway obstruction.

ad b. Upper airway obstruction has been reported by several authors as the cause of serious threats to life during the care of the tracheostomized patient. Of the 310 tracheostomies reported by Nelson and Bowers (1957) the most common complications were "blockage of cannula" and "difficulty with cannula", which occurred in 10 and 7 patients, respectively, in 3 of whom the

outcome was fatal. In 1962 Glas *et al.* found "recurrent respiratory obstruction" in 4 cases out of 80, and Weber (1963) reported dislocation of the cannula in 2 cases out of 400. Quist-Hanssen (1953) stated that "secretory obstruction of the airway with or without secondary lung changes was the most frequent cause of complication and death". Apart from this category of complications, the author mentioned 17 serious cases of "cannular complications", 15 of which consisted of dislocation and 2 of obstruction of the cannula, with a fatal outcome for no fewer than 11 of these in a series of 468 patients. Oliver *et al.* (1962) gave a complication frequency of 2.4% under the heading "tube out or plugged". Aberdeen (1965) reported 4 cases of dislocated cannula in a series of 147 infants, and also severe bronchospasm in 26 cases. For decreasing the tendency to desiccation of secretions in the tracheal cannula and the trachea and bronchi, the "heat-and-moisture exchanger" (Koch *et al.*, 1958, Toremalm, 1960) is of great value.

Ulcerations in the trachea at the level of the tracheostoma, at the site of the inflated cuff and at the site of the lower end of the cannula often occur during treatment with a tracheal cannula, which has been established in post mortem studies by Stiles (1965) and Gibson (1967), among others.

Postoperative haemorrhage can occur as a result of erosion of the anterior tracheal wall and arteria anonyma (Schlaepfer, 1924, Rüedi and Walthard, 1948, Silen and Spieker, 1965), due to a badly fitting cannula. Also given as a cause of haemorrhage is pressure necrosis from an overinflated cuff or one which has been inflated for too long a period (Lord, 1967), especially if infection is present at the same time. A low tracheostomy is also considered more hazardous from the aspect of serious postoperative haemorrhage (Von Schulthess, 1964). Montmollin (1962) observed 1.8% of fatal haemorrhages in a series of 625 tracheostomies. Apart from life-threatening erosional haemorrhages, bleeding can occur as a result of inadequate suturing and mucosal lesions in the trachea caused by the tracheal cannula or lack of care in suctioning. Patients with haemorrhagic diathesis are most vulnerable in this respect. Nelson and Bowers (1957) reported 5 postoperative haemorrhages (+ 5 during the operation), without mortality, in their series of 310 cases, and Meade (1961) reported 7 haemorrhages, one of which was fatal, in his series of 212 cases. Oliver *et al.* (1962) gave a frequency figure of 2.4% for this type of complication, which in their series resulted in 2 deaths.

Infections in the tracheostoma seem to be common (McClelland, 1965) and can spread to the respiratory tract and mediastinum (Head, 1961), or to closely situated operation wounds, which has sometimes proved very serious. Holmdahl and Westerholm (1965) reported that a number of cases of sternal osteitis in association with medial sternotomy had occurred, which were very difficult to treat.

ad c. On decannulation, especially in children, problems often occur, which are usually greater the younger the child. This is well known, and Venables

(1959) reported 12 tracheostomized children below the age of 1 year who proved to be difficult to decannulate and of whom 4 died during attempts at decannulation. ABERDEEN (1965) reported 8 cases of "difficult extubation" and ATKINS (1960) stated that out of 44 tracheostomized children below 12 years of age, as many as 14 left the hospital without being decannulated. The reason for this was not given.

DIAMANT *et al.* (1961) found among 105 tracheostomized children below the age of 10 years 11 patients who offered decannulation difficulties, and the same percentage (9.5%) for this complication was given by OLIVER *et al.* (1962). FEARON *et al.* (1966) claimed that no such problems arose among his series of 504 tracheostomies.

ad d. The most feared of the late complications of tracheostomy is tracheal stenosis. The stenoses described in the literature were caused either by granulation or malacia of the tracheal skeleton or by fibrous scar formations, which are sometimes terminal stages of the two former conditions (MOLLARET *et al.*, 1962, WATTS, 1963, GREISEN, 1966, JOHNSTON *et al.*, 1967).

In a series of 447 tracheostomized patients, MOLLARET et al. (1962) found 36 tracheal stenoses, 21 of which were apparently of the fibrous type. HOFFMANN (1963) gave a frequency of between 5 and 10% for stenotic scar formations after tracheostomy in a thoracic surgical series. EKEDAHL *et al.* (1965) found 4 patients with manifest fibrous tracheal stenosis in a retrospective study of 259 cases in a Swedish hospital. EKEDAHL and LAAGE-HELLMAN (1967) later complemented this study by a follow-up investigation of 41 patients who underwent tracheostomy during one year at the same hospital. Of these, no fewer than 16 patients had minor roentgenological tracheal changes which could be attributed to the tracheostomy, and 4 more pronounced constriction of the lumen of the trachea. One of these patients was a 3-year old child who had

TABLE 4.

Fibrous tracheal stenosis following tracheostomy reported in the literature.

Authors and period of investigation	No. of patients with tracheostomy	No. of patients studied	No. of patients with narrowing of the tracheal lumen to ≥ 50%	No. of patients with marked functional impairment due to tracheal stenosis
MOLLARET *et al.* 1954–1961	912	447		21 (4.7%)
HOFFMAN (1963)	168		(5–10%[2])	
EKEDAHL *et al.* 1960–1964	447	259		4 (1.5%)
KUCHER *et al.* 1960–1966	223	57	13 (23%)	5 (8.8%)
STOECKEL 1962–1967	358	63	16 (25%)	6 (9.5%)
DEVERALL (1967)	104			6 (5.8%)
PEARSON *et al.* 1967	110	43 (50[3])		5(10.0%)

[1]) Not stated whether the narrowing is calculated from the diameter or cross-section area of the trachea.
[2]) Extent of narrowing not stated.
[3]) "Long term survivors".

an intratracheal polyp at the level of the tracheostoma, and in another patient there was a soft constriction of the lumen to the width of a pencil. The other stenoses were of the fibrous type. In a series of 104 tracheostomies extensive tracheal strictures in 6 patients were reported by DEVERALL (1967). KUCHER *et al.* (1967), in a follow-up study of 57 tracheostomized patients, found tracheal constriction by one fourth or more in 42 cases. Tracheal constriction by half the width of the lumen or more was observed in 23% of the patients in the same series, and in a recent report by STOECKEL (1968) the corresponding figure was 25%. Whether the constriction was calculated on the cross-section area of the tracheal lumen or the diameter was not made clear. PEARSON *et al.* (1968) found clinical significant tracheal constriction following tracheostomy and IPPV in 10 out of 50 "long term survivors". In 5 of these patients the respiratory symptoms were pronounced. The frequencies of pronounced fibrous tracheal stenosis after tracheostomy in the studies mentioned above are summarized in Table 4.

The aetiology of tracheal stenosis has been discussed by many authors. It has long been known that with lesions on the first tracheal cartilage and the cricoid ring the risk of subglottic stenosis increases greatly (O'DWYER, 1894, JACKSON, 1921, NELSON *et al.*, 1957, MOLLARET *et al.*, 1962).

Tracheal stenoses which have been reported in recent publications have often been localized, however, to the level of the stoma even if situated well below the first tracheal cartilage. (MURPHY *et al.*, 1966, KUCHER *et al.*, 1967, BRYCE *et al.*, 1968, CHRISTENSEN and DUVALL, 1968, PEARSON *et al.*, 1968). NELSON (1958) discussed the occurrence of tracheal stenosis on the basis of animal experiments, and found that the most important prerequisite for the occurrence of stenosis was "the presence of a cannula". He observed, on the other hand, no definite correlation between the type of incision in the trachea and the degree of subsequent stenosis. MURPHY *et al.* (1966) in animal experiments, found that an inflated cuff which lay partly in the tracheostoma and deformed it could give rise to stenosis at this level. PEARSON *et al.* (1968) has shown that a tracheostoma will always heal with a contracted fibrous scar. This usually means a △-shaped tracheal stenosis in pronounced cases.

GIBSON (1967) and BRYCE *et al.* (1968) have also pointed out the great importance of the inflatable cuff for the occurrence of tracheal lesions which can lead to stenosis. JOHNSTON *et al.* (1967) found among 12 tracheal stenoses after tracheostomy that 7 lay at the level of the cuff of the tracheal cannula, and in a series of 30 tracheal stenoses following tracheostomy PEARSON *et al.* (1968) found $^1/_3$ located in this part of the trachea. CARROLL *et al.* (1969) have studied different types of cuffs for tracheal cannulae and the pressure which they exert on the tracheal wall under different circumstances, and LOMHOLT (1967) has designed a new tracheal cannula in which the cuff pressure against the tracheal wall can be controlled continuously.

Infection in the respiratory tract during the tracheostomy period has been ascribed varying degrees of importance by different authors. STILES (1965)

stated in this respect: "The presence of such infections will increase the damage initiated by aseptic mechanical factors". No parallelism between the occurrence of tracheal stenosis and infections of the respiratory tract was found, on the other hand, by Mollaret *et al.* (1962). Kucher *et al.* (1967) pointed out, however, that infection in the tracheostomy opening and trachea is a regular occurrence and cannot be avoided. These authors were also of the opinion that infections in the tracheostomy area play a role in the occurrence of lesions in the trachea, and Johnston *et al.* (1967) and Gibson (1967) reported that all patients (22 altogether) in their series who had had tracheal stenosis had had infection in the tracheostoma and trachea. In animal experiments Nelson (1958) also concluded that infection in the area in question was of great importance for the occurrence of stenosis.

Prolongation of the tracheostomy period is considered by some authors to increase the risk of lesions in the trachea (Stiles, 1965) and of the occurrence of tracheal stenosis (Mollaret *et al.*, 1962, Greisen, 1966, Ekedahl and Laage-Hellman, 1967). Kucher *et al.* (1967), on the other hand, did not find the duration of the tracheostomy decisive, since many patients in their series of tracheal stenosis had only been tracheostomized for a short period. Further, in half of the 12 patients with tracheal stenosis of Johnston *et al.* (1967), the tracheostomy period was less than 13 days.

Movement of the tracheal cannula, e.g. during respirator treatment, is considered to promote the occurrence of tracheal lesions (Gibson, 1967, Johnston *et al.*, 1967, Bryce *et al.*, 1968).

A high age and diseases which affect the neuromuscular system, such as tetanus, polyneuritis and polyradiculitis, are considered, further, to predispose to tracheal stenosis after tracheostomy (Mollaret *et al.*, 1962, Ekedahl *et al.*, 1965).

Circulatory insufficiency and also disturbances in the fluid balance and other metabolic disturbances can also be of possible importance for the occurrence of lesions (Watts, 1963, Stiles, 1965, Ekedahl and Laage-Hellman, 1967, Pearson *et al.*, 1968, and others).

There are few operations which show such a varying pattern of complications as tracheostomy. It is difficult to find in the literature a clear picture of the total frequency of complications of this procedure, since the data given vary within very wide limits. For children, the complication frequency given by most authors is higher than that for adults.

In Table 5 a summary is given of some of the most common complications of the tracheostomy procedure and those occurring during the care of the tracheostomized patient. Further, the total complication frequency is given in relation to the number of tracheostomies performed, and also the mortality figures. Table 5 is based on information from the publications of twelve authors mainly during the 1940's–1960's. The true frequency of mediastinal emphysema and pneumothorax is quite certainly too low in most of these series, since all

TABLE 5.

Complications and deaths attributed to tracheostomy reported in the literature.

Authors and period of investigation	No. of tracheostomy operations patients)	Mediastinal emphysema	Pneumothorax	Cannula dislodged or plugged	Bleeding	Various other complications	Total complication rate	Death attributed to tracheostomy
			Adults, infants and children					
NELSON and BOWERS 1947–1955	310 (300)	6	7	17	10	14	54 (17%)	16 (5.3%)
HEAD 1947–1959	462	–	4	68	20	97	189 (41%)	4 (0.9%) 22 (4.8%)[1]
MCCLELLAND 1950–1959	389 (383)	–	–	*ca.* 60	–	–	252 (65%)	13 (3.4%)
MEADE 1957–1959	212	3[2]	2	9	7	50	71 (33%)	6 (2.8%)
GLAS *et al.* 1961	80	–	2	4	7	10	23 (29%)	1 (1.3%)
WEBER 1959–1962	400	–	–	2	14	45	61 (15%)	6 (1.5%)
			Infants and children					
NEFFSON 1933–1943	126	30	17	–	–	–	–	10 (7.9%)[3]
FORBES *et al.* 1941–1946	120 (117)	30	12	–	–	–	–	7 (6.0%)[3]
BERGSTRÖM and DIAMANT 1949–1958	74	26	7	–	–	–	–	2 (2.7%)
OLIVER *et al.* 1948–1959	294 (287)	18	17	7	7	–	(31%)[4]	10 (3.5%)
TOREMALM 1958–1959	25	1	0	0	2	4	7 (28%)	0 (0.0%)
The Hospital for Sick Children, Great Ormond Street, London (ABERDEEN, personal communication) 1959–1966	240	0[5]	0[5]	6	2	69	77 (32%)	5 (2.1%)

[1]) The figures denote the number of cases where tracheostomy was a contributory cause to death.
[2]) Including subcutaneous emphysema.
[3]) Death attributed to pneumothorax or emphysema only.
[4]) Percentage of patients with one or more complications.
[5]) Mainly postoperative thoracic surgical cases.

patients did not have a chest X-ray postoperatively. Further, it is clear that all authors have not included late complications such as fibrous tracheal stenosis in giving the total complication frequency.

An exceptionally high complication frequency was reported by MCCLELLAND (1965) who, apart from the figure given in the table, stated that 49.3% of all tracheostomies gave rise to one or more complications, half of which consisted of infection, and a quarter of an obstructed airway. HEAD (1961) also reported a high complication frequency. The series of OLIVER *et al.* (1962) included children below the age of 18 years, and the total complication frequency given here was 31%. In a large recent series comprising tracheostomized children from the Thoracic Unit of the Hospital for Sick Children in London, between

1959 and 1966 (Aberdeen, 1968) the total complication frequency was 32%. This series mainly comprised infants who had undergone thoracic surgical operations.

Apart from the studies included in Table 5 it may be mentioned that Davis *et al.* (1953) stated that among 155 tracheostomies there were as many different complications. These, however, only affected 55 of the tracheostomized patients; over half of the cases were emergency tracheostomies, and the majority of the serious complications affected this category.

In distinct contrast to this high complication frequency is the presentation by Atkins (1960) of 526 tracheostomies, where only 4 complications were reported.

In his monograph on tracheostomy (1964), Von Schulthess reviewed the complications reported in the literature and the experiences of such complications in a series of 1842 tracheostomies. For more detailed discussions of these problems the reader is referred to this study and also to those of Nelson (1958) and Watts (1963).

3. *Mortality*

Tracheostomy is often life-saving, but in view of the related risk to the patient it also involves a certain hazard. The frequency figures for mortality as a direct result of the operation or complications during or after the period of tracheostomy vary greatly in different reports. In the investigations summarized in Table 5 the mortality in tracheostomy lay between 0 and 7.9%.

Apart from the high mortality (7.9%) reported by Neffson (1943), there is no definite difference in mortality in these series between those which comprised both infants, children and adults and those comprising infants and children alone.

"Operative complications" constituted the cause of the majority of deaths in the series presented by Nelson and Bowers (1957), but in 10 cases these meant "errors in surgical judgement and delay in undertaking a clearly indicated tracheostomy". Head (1961) stated that in addition to the 4 deaths which were due directly to the tracheostomy, there were 22 cases where the tracheostomy was a contributory cause of death. Meade (1961) reported that 5 deaths out of 6 occurred in the postoperative period, and Weber (1963) gave postoperative haemorrhage as the predominant cause of death. Mediastinal emphysema and pneumothorax were the cause of all deaths reported in the publications of Neffson (1943), Forbes *et al.* (1947) and Bergström and Diamant (1959). Oliver *et al.* (1962) reported the same number of deaths in connection with the operation as postoperatively. In Toremalm's series (1960) no deaths occurred as a result of tracheostomy.

Some further mortality figures from other recent publications may be mentioned, viz. Atkins (1960) 0.4%, Watts (1963) 1.4%, Dugan and Samson (1963) 1.1%, Lord (1967) 1.1% and Deverall (1967) 3%.

In the presentation by Toremalm (1960) of the tracheostomy series of nine authors, a mortality of 2–13% is reported for children below the age of 10 years. Fearon *et al.* 1966 reported a mortality of only 0.4% in a paediatric series comprising 504 tracheostomies. Aberdeen and Glover (1967) wrote: "Our personal experience at this unit is now more than 200 cases of tracheostomy, two thirds of these in the first 3 months of life", and continued: "the ultimate survival rate was only one third, but in only 5 cases (i.e. less than 3%) could a complication of tracheostomy be considered as a significant cause of death".

C. *Advantages of prolonged endotracheal intubation compared with tracheostomy*

Prolonged endotracheal intubation and tracheostomy have in many respects the same weaknesses and often provide the same possibilities. As an alternative to tracheostomy, however, endotracheal intubation has a number of advantages:

1. Endotracheal intubation is usually a simple procedure which is relatively free of risk and can be carried out quickly.

2. In the case of displacement and blockage of the endotracheal tube it is always possible to remove the tube immediately in order to produce rapidly a free airway.

3. After extubation the possibility remains of reintubating the patient quickly if necessary. On decannulation of a tracheostoma, this usually shrinks rapidly, making replacement of the cannula impossible, and because of this difficulty there is a tendency, "to be on the safe side", to retain a tracheostomy for a longer period than is absolutely necessary. Because of this a patient who needs to be treated with IPPV for one day, for example, may keep his tracheostomy for several days, which may increase the risk of complications.

4. Immediate operative complications are avoided. The risk of these is often underestimated but constitutes a reality, which is evident in reports of all large investigations of these problems. Haemorrhage, subcutaneous and mediastinal emphysema, pneumothorax, air embolism, damage to the cricoid cartilage and first tracheal ring, posterior tracheal perforation, damage to the recurrent laryngeal nerve and foreign body in the tracheobronchial tree have all been reported (Watts, 1963, Von Schulthess, 1964).

5. The use of prolonged endotracheal intubation avoids possible intratracheal cicatricial stenosis as a sequela of a healed tracheostoma.

6. The risk of cross infection between an infected tracheostoma and a closely situated operation wound, e.g. medial sternotomy, is eliminated (Holmdahl and Westerholm, 1965).

D. *Disadvantages of prolonged endotracheal intubation compared with tracheostomy*

In certain respects prolonged endotracheal intubation has disadvantages which tracheostomy lacks, and the most important of these will be mentioned briefly below:

1. Specific laryngeal lesions can be caused by an endotracheal tube and can give rise to residual damage.

2. The discomfort of an endotracheal tube in conscious patients is usually greater than that of a tracheal cannula, although some authors have reported surprisingly good tolerance in some patients (Dammann, 1965, Atherstone and Ryder, 1967, Hansen and Jørgensen, 1968). Infants also generally accept an endotracheal tube well (Allen and Steven, 1965).

3. Accumulation of inspissated or dried secretions has a greater tendency to occur in an endotracheal tube than in a tracheal cannula, and suction is generally considered more difficult via an endotracheal tube. With adequate humidity of the inspired or insufflated air, however, this does not seem to be a great problem.

4. There is a possibility that an endotracheal tube may slide down into the right primary bronchus and cause atelectasis in the left lung.

The causes of the disadvantages under point 1 have not been fully investigated and this has resulted in some uncertainty as to the consequences of the method; criteria for evaluation of the risk of late lesions would seem desirable (Fearon *et al.*, 1966, Harrison and Tonkin, 1968, Minnigerode, 1968).

Chapter II

MATERIAL

A. *Principles followed in the collection of the series*

1. The patient should have been admitted to the University Hospital, Uppsala, and have been intubated for a continuous period of more than 24 hours between the years 1964 and 1967.

2. The patient should have undergone direct or indirect laryngoscopy by the author within one week after the extubation. For those patients who died during the intubation period the larynx and trachea should have been subjected to post mortem examination.

3. Relevant information concerning intubation and care of the patient during the intubation period should have been noted on a special card by the nurse on duty, in consultation with an anaesthetist, in the intensive care unit, or should have been available in the original case journal.

ad. 2 For practical reasons it was not possible to include all patients who were intubated for 24 hours or more during the period in question. With the following exception only those patients whom it was possible for the author himself to examine after the intubation period were included. The exception was made for about 10% of the thoracic surgical patients for whom during the first stage of the investigation the anaesthetist gave information on the laryngeal status at extubation; these patients were also included.

ad. 3. It was not always possible for relief nurses working for a short time in the intensive care units to be informed about the notes to be made on the special card, as mentioned above. For this reason, which resulted in deficiency of certain data, a further number of patients were excluded from the investigation.

B. *Composition of the series*

The above criteria were fulfilled by 457 patients. A schematic classification of this series is given in Fig. 1. 79 patients died during the primary period of hospitalization. In these cases the larynx and trachea were subjected to post mortem examination. This latter series will be referred to in the following as "the post mortem series". All patients who were discharged from the hospital after the primary period of hospitalization were requested to come for follow-up examination.

The following patients could not be followed up:

1. At the time of notification of the follow-up examination a further 43 patients had died. The death certificates for these patients were checked and in no case were lesions in the larynx or trachea given as the cause or contributory cause of death.

2. Six patients gave different reasons for not attending the follow-up examination, and in 21 patients this examination could not be performed because of geographical

circumstances. A questionnaire was sent to all these patients with questions as to whether they had had hoarseness or other symptoms from the upper respiratory tract since they left hospital. 18 patients replied, and none of these reported symptoms which could be related to damage occurring during the intubation period. The other 9 did not reply. No requests had been made from other hospitals for case notes or information concerning these patients, however, and it was therefore assumed that no serious complications had occurred in these cases either.

A follow-up examination was performed on 312 patients, referred to in the following as "the follow-up series" (Fig. 1). Of these patients, 4 died before being discharged after the primary period of hospitalization, and they are therefore also included in the post mortem series. Within the follow-up series, the second half of the patients were classified at the first examination after extubation with respect to acute lesions after prolonged intubation. This group is called F_1 (161 patients). Within group F_1 a group of patients was repeatedly studied with regard to the healing course for the acute lesions. This group is called F_2 (100 patients) (Fig. 1), and consisted of those patients in group F_1 who lived in Uppsala or in places with good communication with Uppsala so that at the repeated examination they were able to return home within the same day.

Patients of 16 years of age and over are called "adults". "Infants and children" were below 16 years of age at the time of intubation.

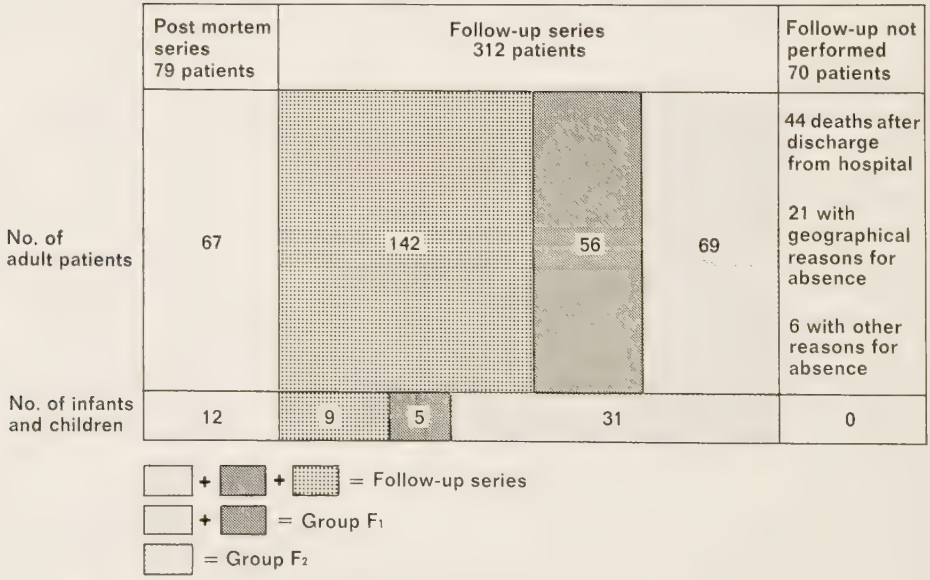


FIG. 1.—Total series of 457 patients. 4 patients are included in both the follow-up and the post mortem series, which explains why the sum of the different groups exceeds the total series by 4.

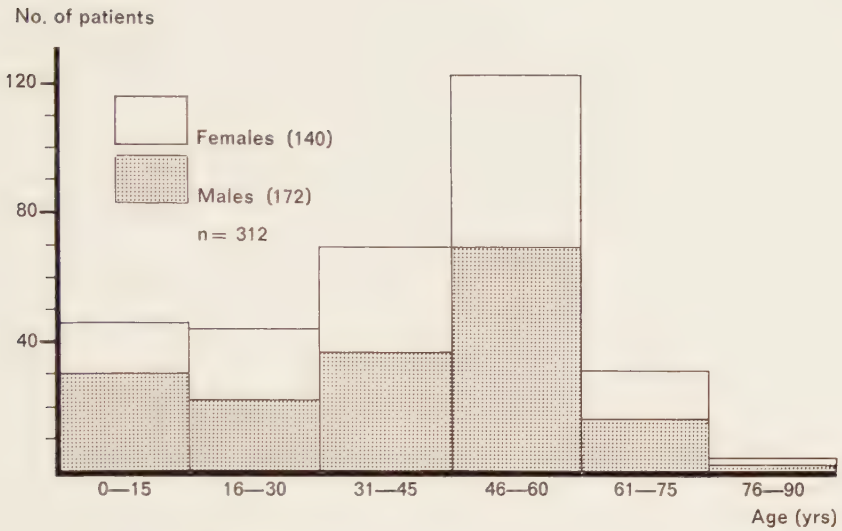


FIG. 2.—Age and sex distribution in the follow-up series.

Fig. 2 shows the age distribution of the follow-up series. The corresponding distribution for the post mortem series is given in Fig. 3.

Figs. 2 and 3 also show the sex distributions within the different age groups.

In the follow-up series, 39% were between 46 and 60 years old at the time of intubation, and the median age was 45 years. Of the children, 44% were

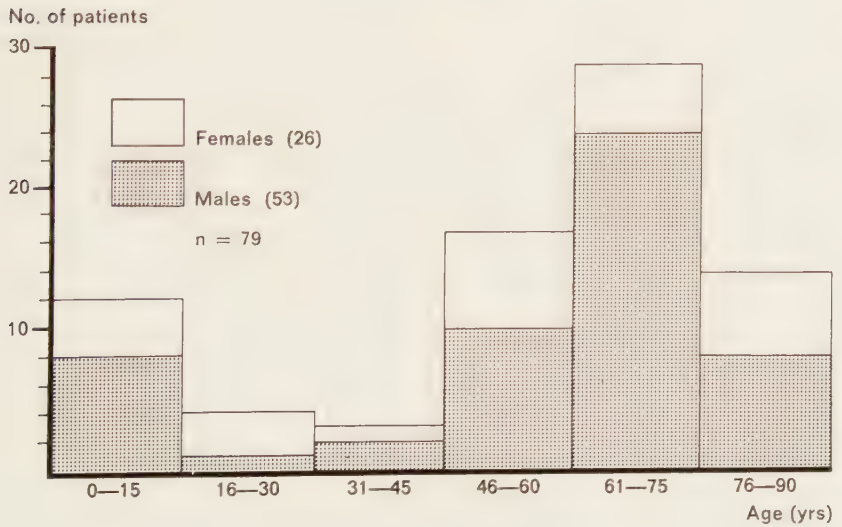


FIG. 3—Age and sex distribution in the post mortem series.

Table 6.

Age distribution in different groups formed by indication for prolonged endotracheal intubation in the follow-up series.

Age Groups (Years)	Postoperative respiratory deficiency or insufficiency		Drug poisoning	Miscellaneous[1])	No. of patients
	Thoracic surgery	General surgery			
0–15	19	13	1	12	45 (14%)
16–30	23	1	15	5	44 (14%)
31–45	55	1	7	5	68 (22%)
46–60	110	2	5	5	122 (39%)
61–75	15	5	2	8	30 (10%)
76–90	–	2	–	1	3 (1%)
No. of patients	222	24	30	36	312 (100%)

[1]) Details of the miscellaneous indications are given in Table 9.

below the age of 1 year at the time of intubation, and the median age in this group was 2 years.

The majority of patients (37%) in the post mortem series were in the age group 61–75 years. The median age for this series as a whole was 63 years. The post mortem series of children was relatively small and consisted mainly of infants below the age of 1 year. The median age in this group was 4½ months.

A deviation towards higher ages was thus noted in the post mortem series (Fig. 3) in comparison with the follow-up series (Fig. 2).

Table 7.

Age distribution in different groups formed by indication for prolonged endotracheal intubation in the post mortem series.

Age Groups (Years)	Postoperative respiratory deficiency or insufficiency		Drug poisoning	Miscellaneous[1])	No. of patients
	Thoracic surgery	General surgery			
0–15	–	3	–	9	12 (15%)
16–30	–	–	2	2	4 (5%)
31–45	1	–	–	2	3 (4%)
46–60	3	6	–	8	14 (21%)
61–75	2	12	–	15	29 (37%)
76–90	–	9	–	5	14 (18%)
No. of patients	6	30	2	41	79 (100%)

[1]) Details of the miscellaneous indications are given in Table 10.

The mean age for the former series was 53.23 years (SD = 27.30; range: 1 day to 76 years) and for the latter 40.55 years (SD = 19.40; range: 1 day to 89 years).

Table 6 gives the age distribution in the follow-up series with regard to the following four classifications: thoracic surgery, general surgery, drug poisoning and miscellaneous indications. Almost half (49%) of the thoracic surgical patients were within the age group 46–60 years. The general surgery group was smaller and the mean age higher, which is in good agreement with the experience that the need for postoperative artificial ventilation in this group is greatest in older persons. Half of the patients in the drug poisoning group were 16–30 years old. The miscellaneous group, finally, consisted mostly of children. The diagnoses in this group are given in Table 9.

In Table 7 the age distribution is given for the post mortem series with regard to the same four classifications as given above for the follow-up series. The diagnoses in this series were more numerous than in the follow-up series, and are given in Table 10.

Brief reports of cases included in the post mortem and follow-up series are available in the University Library of Uppsala.

Chapter III

METHODS

A. *Methods applied in prolonged endotracheal intubation*

1. *Indication for prolonged endotracheal intubation and principles in determination of length of intubation period*

Common to all the patients reported here—except for some patients unconscious due to drug poisoning—is that prolonged endotracheal intubation was carried out where otherwise, before this method was introduced, tracheostomy would have been performed. In the great majority of patients the reason for prolonged intubation was an expected or manifest respiratory insufficiency which required treatment with a respirator. In evaluating the respiratory insufficiency or the risk of hypoventilation, at the University Hospital in Uppsala during the period of this study, certain previously defined norms were followed, and the reader is referred in this respect to the following publications: Controlled Ventilation in Medical Practice (Norlander, Björk, Crafoord, Friberg, Holmdahl, Swensson, Widman, 1961); The Respiratory Care Unit

Table 8.

Duration of endotracheal intubation in adult patients and infants and children in the follow-up and post mortem series.

Duration of intubation (hrs)	Follow-up series		Post mortem series		No. of patients
	Male	Female	Male	Female	
	Adults				
24–35	115	102	15	10	242
36–47	13	8	9	4	34
48–59	6	8	8	3	25
60–71	3	3	5	3	14
72–	4	5	8	2	19
No. of patients	141	126	45	22	334
	Infants and children				
24–35	11	6	2	1	20
36–47	4	2	1	1	8
48–59	5	1	–	2	8
60–71	1	1	–	–	2
72–	10	4	5	–	19
No. of patients	31	14	8	4	57

(Holmdahl, 1962); Respirator Treatment for Hypoventilation Following Thoracic Surgery (Björk and Holmdahl, 1965).

The durations of endotracheal intubation for patients in the follow-up and post mortem series are given in Table 8. Adult patients in the follow-up series had an endotracheal tube for a mean period of 32 hours (SD = 20 hours, range: 24–205 hours), and infants and children of the same series 71 hours (SD = 81 hours, range: 24–504 hours). In adult patients of the post mortem series the corresponding mean value was 48 hours (SD = 23 hours, range: 24–154 hours) and in infants and children of this latter series 73 hours (SD = 56 hours, range: 24–209 hours).

Extubation was usually performed after 24 hours in conscious adult patients; in these patients drugs had been administered to assist their toleration of the tube. If after this length of time it was considered that the patient would need further artificial ventilation for 2 or 3 days, the tube was allowed to remain *in situ* for this period. If, on the other hand, it was predicted that more prolonged artificial ventilation would be required, secondary tracheostomy was performed already after the first 24 hours of intubation.

In children, prolonged intubation was used, as a rule, for up to one week if a considerably longer need of artificial ventilation had not been predicted. After this period of time secondary tracheostomy was usually considered to be indicated if the child needed further respirator treatment or was unable to maintain a free airway spontaneously.

Before extubation, care was taken to see that the effect of muscle relaxants and sedatives had been eliminated.

Primarily unconscious patients were kept intubated for 2–3 days, after which secondary tracheostomy was performed if there were no signs of improvement. In cases of drug poisoning a longer intubation period was allowed in view of the possible psychological consequences of a tracheostomy scar in these patients. The tube was removed when the cough and swallowing reflexes had returned. In adults, tracheostomy was performed with a transverse incision through the skin and with a flap as described by Björk (1960), and in children with a transverse incision through the skin and a longitudinal incision through tracheal rings 2 and 3 and in some cases 4.

It was not an aim of this investigation to study the indications for prolonged intubation. The condition of the patient plays a role, however, as regards tolerance of the tube, and therefore information concerning diagnosis and status is of some importance.

In the follow-up series postoperative artificial ventilation was given to 245 patients, 69 patients had received respirator treatment because of respiratory insufficiency not connected with surgery and only 8 patients had been intubated to ensure a free airway on spontaneous breathing. The frequencies of secondary tracheostomies in children and adults were 27% and 17%, respectively (Table 9).

In the post mortem series postoperative respirator treatment was given to 36 patients and respirator treatment for reasons not connected with surgery to 41 patients; intubation alone was used in 2 patients. The frequency of secondary tracheostomies in this series was 17% for children and 55% for adults (Table 10).

TABLE 9.

Distribution of patients in the follow-up series according to indications for prolonged endotracheal intubation, respirator treatment and secondary tracheostomy.

Indication for treatment	Prolonged endotracheal intubation No. of patients		Respirator treatment No. of patients		Secondary tracheostomy[1] No. of patients	
	Adults	Infants and Children	Adults	Infants and Children	Adults	Infants and Children
Postoperative respiratory deficiency or insufficiency:						
Thoracic surgery	203	19	203	18	30	5
General surgery	11	13	11	13	4	3
Drug poisoning	29	1	24	1	5	
Bronchial asthma	8	1	8	1	1	–
Bronchial asthma + Bronchopneumonia	1	–	1	–	1	–
Exacerbation of chronic pulmonary disease	3	–	3	–	1	–
Myocardial infarction	1	–	1	–	–	–
Cardiac failure	3	–	3	–	–	–
Pulmonary oedema	1	–	1	–	1	–
Pancreatitis + Delirium tremens	1	–	1	–	–	–
Epilepsy	1	1	1	1	–	–
Myasthenia gravis	1	–	1	–	1	–
Bronchopneumonia	–	2	–	2	–	1
Epiglottitis	–	2	–	2	–	–
Meningitis	–	1	–	1	–	–
Skull injury	2	2	2	1	1	1
Gunshot wound	1	–	1	–	1	–
Reticuloendothelioma	–	1	–	1	–	–
Sturge-Weber syndrome	–	1	–	–	–	1
Congenital malformation + Respiratory insufficiency	–	1	–	1	–	1
Allergic oedema	1	–	1	–	–	–
No. of patients	267	45	262	42	46	12

[1]) Reasons for secondary tracheostomy are given in Tables 16 and 17.

In the follow-up series the thoracic surgical patients were in the great majority, while in the post mortem series the general surgical patients predominated. This is partly connected with the fact that those patients who had been intubated after general surgical operations were often severely and acutely ill, often elderly and sometimes in deep shock. Furthermore, in certain groups of the thoracic surgical patients, so called prophylactic respirator treatment was used to a greater extent than in the general surgical patients (BJÖRK and HOLMDAHL, 1965).

The mortality within the different indication groups could not be calculated from comparisons between the follow-up series and the post mortem series, since the frequency of laryngotracheal specimens taken from patients who died was different in the thoracic intensive care unit and the general intensive care unit.

TABLE 10.

Distribution of patients in post mortem series according to indications for prolonged endotracheal intubation, respirator treatment and secondary tracheostomy.

Indication for treatment	Prolonged endotracheal intubation No. of patients		Respirator treatment No. of patients		Secondary tracheostomy[1] No. of patients	
	Adults	Infants and Children	Adults	Infants and Children	Adults	Infants and Children
Postoperative respiratory deficiency or insufficiency:						
Thoracic surgery	6		6		5	-
General surgery	27	3	27	3	13	
Drug poisoning	2		2		1	-
Bronchial asthma	1		1		-	
Chronic pulmonary disease + Bronchial asthma	4		4		3	
Exacerbation of chronic pulmonary disease	1		1	-	1	-
Myocardial infarction	5		5	-	1	
Cardiac infarction + Sepsis	1		1		1	-
Cardiac failure	1		1	-	1	
Pulmonary oedema + Pneumonia	1		1			
Pulmonary embolism	1		1		1	
Cardio-arterio-nephro-sclerosis	1		1		1	
Uraemia	1		1		1	
Pyelonephritis + Cerebral oedema		1		1		
Peritonitis	1		1		1	
Chronic cholecystitis with abscess perforation	1		1		-	
Subarachnoid haemorrhage	4		3			
Multiple sclerosis	1		1		1	
Acute encephalitis		1		1		
Meningococcal sepsis		1		1		
Bronchopneumonia		1		1		1
Bronchopneumonia + Cardiac failure	1				1	
Skull injury	1	1	1	1	-	
Other traumatic injuries	2		2		1	
Diabetes mellitus + Cerebral oedema and cerebral haemorrhage		1		1		
Chronic lymphatic leukaemia	1		1			
Bronchogenic carcinoma + Bronchopneumonia	1		1		1	

[1]) Reason for secondary tracheostomy was expected prolonged respirator treatment in all cases.

Table 10 (cont.).

Indication for treatment	Prolonged endotracheal intubation No. of patients		Respirator treatment No. of patients		Secondary tracheostomy[1]) No. of patients	
	Adults	Infants and Children	Adults	Infants and Children	Adults	Infants and Children
Carcinoma of the breast with metastasis + Cardiac failure	1	–	1	–	–	–
Malignant tumor	1	–	1	–	–	–
Congenital malformation + Respiratory insufficiency.	–	1	–	1	–	1
Erythroblastosis foetalis	–	1	–	1	–	–
Immaturitas	–	1	–	1	–	–
No. of patients	67	12	65	12	34	2

[1]) Reason for secondary tracheostomy was expected prolonged respirator treatment in all cases.

2. *The endotracheal tube*

In the main, three types of endotracheal tubes were used:

1. A Magill red rubber tube (manufactured by Franklin, England and Rüsch, Germany).

2. BOC and Flotex nylon reinforced latex tubes (manufactured by British Oxygen Company Ltd., England, and Eschmann Bros. & Walsh Ltd., England, respectively).

3. A Portex polyvinyl chloride (PVC) tube (manufactured by Portex Ltd., England).

Cuffed tubes were used, as a rule, when the inner tube diameter exceeded 5 mm. Below this size uncuffed tubes were chosen. In nasal intubation of small children and infants, the PVC tube modified by Jackson Rees and Owen-Thomas (1966) was used during the second half of the period covered by this investigation. All measurements for inner and outer tube diameters were given in millimeters by the manufacturers.

The sizes (external diameters) and materials of the tubes used for adult patients in the follow-up series (243 patients) and the post mortem series (52 patients) in those cases where only one type of tube was used are given in Figs. 4 and 5. Tubes of two different materials and/or external diameters were used for 18 adult patients in the follow-up series and 11 patients in the post mortem series. Further, in 1 patient 3 different types of tubes were used, and for 5 patients in the follow-up series and 3 patients in the post mortem series no information was available as to the tube diameter or material.

The sizes and materials of the tubes used in 44 of the 45 infants and children of the follow-up series and the 12 infants and children of the post mortem series are shown in Figs. 6 and 7. For 1 child in the follow-up series there was no information in this respect. In 9 patients in the follow-up series and 2 patients in the post mortem series tubes of different material and/or with different external diameters were used, and in these cases the tube with the largest external diameter was always noted in the figure.

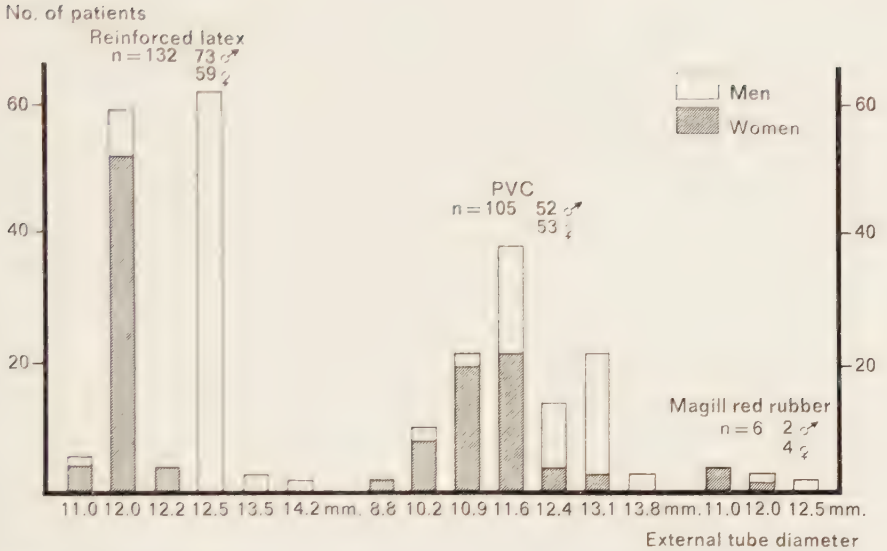


FIG. 4.—External tube diameter and tube material in adult patients treated with one kind of tube only, in the follow-up series.

In a number of patients more than one type or size of tube was used for short periods. Only tubes used for 8 hours or more were recorded, however.

3. *Technique of intubation*

Intubation was performed under ocular control with the aid of a Macintosh laryngoscope with a curved blade, except in the neonatal period when a straight blade was sometimes used.

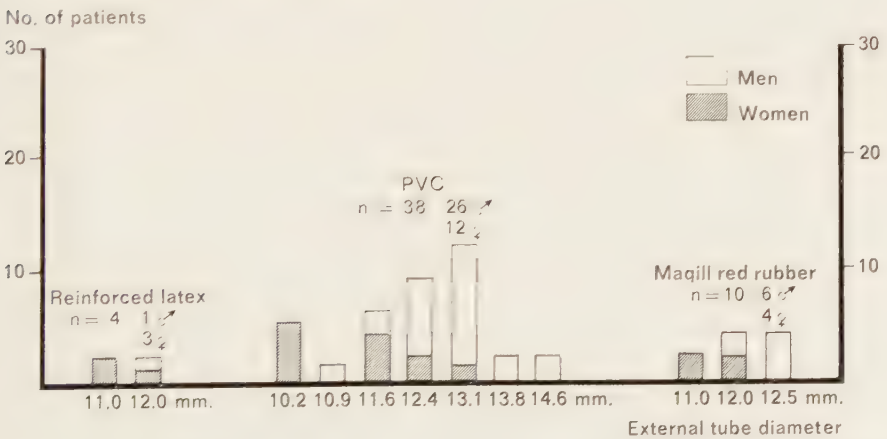


FIG. 5.—External tube diameter and tube material in adult patients treated with one kind of tube only, in the post mortem series.

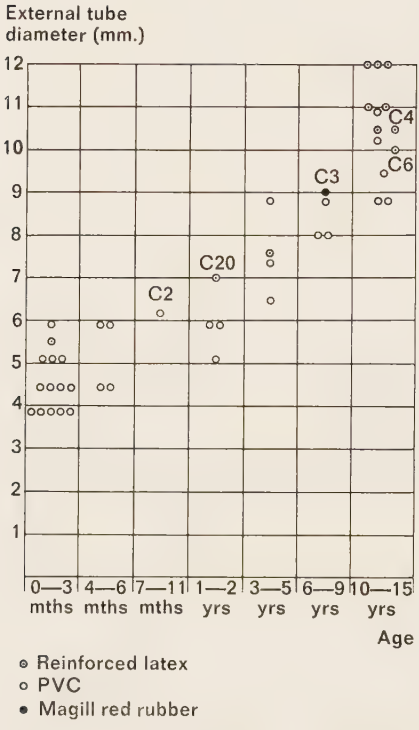


Fig. 6.—Size and material of tube in different age groups of infants and children in the follow-up series. The case numbers are noted above patients who were tracheostomized after extubation because of respiratory obstruction caused by acute lesions due to the endotracheal tube. Cases C 2 and C 20 healed with subglottic fibrous stenosis and case C 3 with a fibrous glottic web.

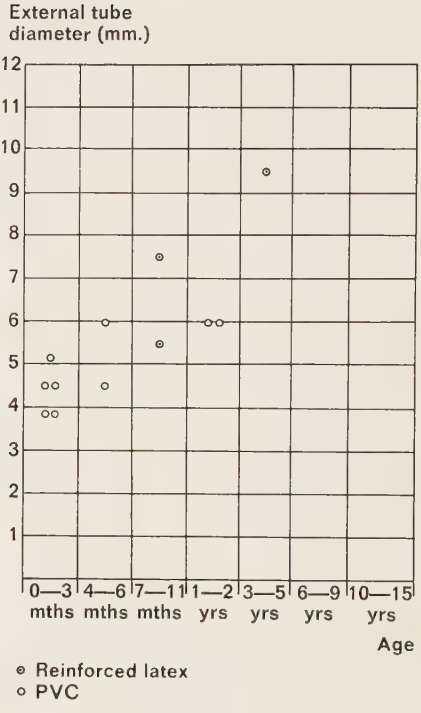


Fig. 7.—Size and material of tube in different age groups of infants and children in the post mortem series.

The postoperatively treated patients were intubated on induction of anaesthesia and generally the same tube was left *in situ* after the operation. If the tube was too large or of an unsuitable material (red rubber), it was exchanged at the end of the operation for one of reinforced latex (mostly BOC) or of PVC (Portex).

In non-postoperative respiratory insufficiency the patient was intubated immediately after admission to hospital, generally by an anaesthetist but in a few cases by the medical intern on duty. Magill red rubber tubes were usually used but were most often exchanged for PVC (Portex) tubes when the patient arrived at the intensive care unit. In a few cases, however, the primarily used Magill red rubber tube was allowed to remain *in situ* for the entire intubation period.

The tube was changed daily at the beginning of the investigation period, when prolonged intubation had only recently been introduced and was less frequently used. When the tube was changed the larynx was examined by the anaesthetist on duty, for any lesions which might have occurred. During the later part of the investigation period the tube was usually left *in situ* unless there were any special indications for changing it, i.e. signs of incipient tube occlusion.

In patients with absent reflexes and in many infants in the neonatal period intubation was performed without muscle relaxants. In adult patients and children with normal reflexes, suxamethonium chloride (Celocurin®) or d-tubocurarine chloride (Tubarine®) were used as muscle relaxants. Children less than 2–3 years old were sometimes anaesthetized with an N_2O+O_2+ Halothane mask to a depth at which the laryngeal reflexes were eliminated.

The doctor performing the intubation always aimed at using en endotracheal tube which he considered easily passed through the larynx. If there was any doubt about this, the tube was usually changed to one with a smaller diameter. Since in the general intensive care unit the number of doctors who performed intubation was large, the assessment of the size of the tube in relation to the lumen of the larynx was less uniform there than in the thoracic intensive care unit where, with a few exceptions, the same anaesthetist intubated the patients and tended them postoperatively from an anaesthesiological aspect.

In adults, with a few exceptions, intubation was performed perorally. In children the intubation route varied, but the nasal route was preferred to an increasing extent. Before intubation was performed through the nose, the patient was always first intubated orally to enable a suitable tube size to be chosen.

The endotracheal tube was carefully fixed with adhesive tape. When tubes of the types modified by Jackson Rees and Owen-Thomas were used, fixation was produced by the same method, in principle, as described by these authors in 1966 and which is illustrated in Fig. 8.

4. *General care of the intubated patient*

Every patient with prolonged intubation was supervised continuously by a special attendant with short theoretical and practical training with respect to respirator treatment and the care of intubated and tracheostomized patients. The attendant was instructed to call the head nurse on duty in the intensive care unit immediately if there were any signs of airway obstruction. Increasing insufflation pressure on ventilation with a volume-controlled respirator constituted a reliable warning signal in this respect.

Changes in pulse rate, blood pressure and facial colour were further reasons for a check by the more qualified staff. In patients in a poor condition, ECG was recorded continuously on an oscilloscope.

FIG. 8.—Case C 48: 4½-month old girl operated on for oesophageal atresia and postoperatively ventilated via a Jackson Rees endotracheal tube. The figure shows the fixation of the respirator tubes to the patient's head and their connection to the endotracheal tube.

The Engström respirator (LKB Medical AB, Bromma, Sweden) was used exclusively in the series of the present investigation.

When necessary for adjustment of the respirator, the adequacy of ventilation was checked by analysis of the arterial blood with respect to O_2 and CO_2 pressure.

The cuff of the endotracheal tube was kept inflated to such an extent that there was only a very slight leakage with the insufflation pressure used. It was not deflated regularly.

The insufflated or inspired air was humidified in different ways. Patients who were breathing spontaneously were provided with a heat-and-moisture exchanger as described by TOREMALM (1960). In many infants who were breathing spontaneously during some part of the intubation period the inspired air was humidified according to the "vapor tent principle" by means of an ultrasonic nebulizer or by some other form of air humidifier (mostly Defensor 505, Defensor, Switzerland). The standard humidifying unit on the Engström respirator was used during the first half of the investigation period to humidify the insufflated air (the gas mixture). During the second half of the investigation period air humidification was produced to an increasing extent by an ultrasonic nebulizer (LKB Medical AB, Bromma, Sweden) incorporated into the gas circuit (HERZOG *et al.*, 1964). Because of lack of apparatus, however, even during this period all adult patients did not have the latter type of air humidification. All children, on the other hand, were given this treatment.

After extubation all children lay in a vapor tent for 1 or 2 days. When possible the air was humidified by an ultrasonic nedulizer; otherwise the type

of air humidifier mentioned above was mainly used. The adult patients did not usually lie in a vapor tent but to the greatest possible extent a nebulizer was placed in the room in order to raise the relative humidity of the atmospheric air, which during the winter in the intensive care units was very dry (the relative humidity was sometimes as low as 20%) without active air humidification. Cleaning of the endotracheal tube by suction was performed with sterile catheters. In adults, disposable sterile plastic Nelaton catheters (Mediplast, Sweden) were used and only exceptionally rubber catheters of the same type. In children, plastic feeding-tubes (Bardic, USA) were generally employed.

Suction was performed only when necessary. In doing this, the catheter was inserted no further than was absolutely necessary, in order to protect the tracheal and bronchial mucosa. Sterile saline solution was usually dropped into the tube at the time of suctioning. When an ultrasonic nebulizer was used for air humidification, this was not necessary, however, since under these conditions the respiratory tract was adequately moistened.

Muscle relaxants and sedatives were only given to patients who were conscious or who had considerable laryngeal motor activity, while unconscious patients with no convulsions, e.g. patients with traumatic skull injuries, cerebral accidents or drug poisoning, were given no such medication for reason of the endotracheal tube and/or respirator treatment. Adult surgical patients were given d-tubocurarine chloride (Tubarine®) during the surgical operation, and the curare effect was allowed to persist after completion of the operation. A few adult patients were even kept curarized throughout the postoperative respirator treatment. Usually, phenoperidine (Lealgin®) was given in doses of 2 mg intravenously from the time when the patient began to react to the endotracheal tube or had difficulties in following the respirator frequency. The frequency of administration of phenoperidine depended upon the reaction of the patient, which usually meant that it was given at intervals of 4 hours. It was never given later than 5 hours prior to extubation. Adult patients who were treated with a respirator for causes other than surgical intervention were usually curarized initially and subsequently given the same medication, in principle, as the postoperative group.

Older children were, on the whole, treated with the same regimen as the adults. Small children up to the age of 3–4 years were, as a rule, kept curarized during the intubation period, and were at the same time sedated with haloperidol (Haldol®) or given an N_2O-oxygen mixture to inhale. To a minor extent, however, phenoperidine was also tested in this age group. In infants in the neonatal period, the endotracheal tube gave no reason for drug administration, since it was found that after an initial period of about an hour they tolerated the tube very well.

When spontaneous respiration was considered desirable in children during the intubation period, only sedation with haloperidol was used.

Antibiotics were not given as routine during intubation and/or respirator treatment. Most of the postoperative patients and many of those who were

treated with prolonged intubation for reasons other than surgical intervention were, however, given intensive antibiotic therapy for other reasons both during and after the period of intensive care.

Cortisone was given mainly to asthma patients, as a rule both during and after the period of intubation.

The fluid balance and electrolyte status were checked daily as routine. Disturbances in these respects were corrected immediately as far as possible. In cases of drug poisoning, 5 litres of fluid were usually given per day during the time of unconsciousness, provided that the renal function was normal.

Chest X-ray was performed daily during the intubation period.

B. *Methods used in the study of the consequences for the larynx and trachea*

1. *Principles used in recording important data of the patient*

From the time at which the patient arrived at the intensive care unit, a special card was filled in side by side with the routine case journal. On this special card the nurse in charge of the patient, in consultation with the anaesthetist, noted the time of intubation, the size and material of the tube, and the intubation route. Further, it was noted whether the intubation procedure had been easy or difficult, if it had been performed under emergency conditions or if special problems had occurred on intubation.

The times of respirator treatment were recorded, and any medication with muscle relaxants or sedatives during the intubation period were entered on the card.

The times of chest X-rays were also noted, and finally also the time of extubation.

With regard to the objective tolerance of the endotracheal tube, only unusual deviations were noted, since the patient was controlled by means of muscle relaxants and sedatives in this respect.

After the intubation period, data were noted by the author on the special card with respect to initial lesions, the healing course for a number of these lesions, the findings at the follow-up examination and information given by the patient at this examination.

2. *Laryngoscopy*

When the larynx was inspected immediately after extubation, this was done with a Macintosh laryngoscope.

When the patient was extubated without immediate inspection of the larynx, indirect laryngoscopy was performed within one week after the extubation and usually several times within that week.

At the follow-up examination all patients underwent indirect laryngoscopy. Direct laryngoscopy was performed when pathological changes, requiring

further investigation, had been established and in some cases where, despite local anaesthesia, indirect laryngoscopy did not give an adequate view of the larynx.

In group F_2, where studies were made with regard to the healing course of initial intubation lesions, about half of the patients also underwent direct laryngoscopy in connection with repeated photographic recordings of the changes (see under (3) below). In these patients follow-up examinations were performed approximately every 15 days until the lesions had healed.

Direct laryngoscopy was performed under pentothal anaesthesia and celocurin apnoea after the patient had first inhaled 100% O_2 for about 5 minutes.

3. *Photographic recording*

Typical reactions, lesions, the healing course and the sequelae in the larynx and trachea after prolonged intubation were recorded photographically. Direct laryngoscopy and tracheoscopy were performed with a Storz pharyngolaryngoscope and a bronchoscope, respectively, supplied with straight-vision photo optic and with the relevant standard photographic equipment. Kodak Ektachrome-x film for daylight or blue flash was used.

4. *Chest radiography and radiographic study of the trachea and larynx*

Chest radiography was performed and the results were evaluated by a radiologist. The first examination was carried out immediately after the intubation or, in postoperative cases, immediately after completion of the operation, in most patients as a bedside examination. The state of the lung parenchyma was assessed and results from at least two radiographic examinations with an interval of at least one day were studied. In the absence of parenchymal changes the results were called "normal". When parenchymal changes had been observed at the first examination and these remained unchanged, this was denoted "unchanged". New parenchymal changes or such changes which had increased were denoted "progression", and parenchymal changes which had decreased or disappeared were denoted "regression". In cases where the parenchyma showed a varying picture during a series of radiographic examinations, this was denoted "variable". Pleural changes and changes which were considered to be due to vascular stasis were not included.

Radiography of the trachea was performed at the follow-up examination. The purpose of this examination was to reveal intratracheal stenosis. Exposures were made in the frontal plane, sagittal plane and at a rotation of 45°. The customary radiographic technique was used and the results were evaluated by a radiologist. Patients with positive findings were subjected to further radiographic examinations, usually including tomography.

In order to assess the relative degree of tracheal stenoses observed, the following procedure was used: From the lateral and frontal films of the

trachea, the smallest cross-section area (S_{min}) was calculated and correlated to the mean value (S) of the cross-section areas 2 cm above and 2 cm below the stricture. The lumen was assumed to be constant and to have the form of an ellipse both in a stenosis and in a normal trachea. The following equation was used: $C = \frac{S - S_{min}}{S} \cdot 100$, where C is the constriction expressed in per cent of the lumen of the trachea. The shape of the cross-section of the trachea and of a stricture varies from one patient to another and thus constitutes a source of error. The pronounced fibrotic stricture is probably unchanged by different respiratory phases, while the normal tracheal lumen can vary in these phases. In order to eliminate as far as possible the effect of possible repiratory variations of the trachea, measurements of the stricture and tracheal lumen were made on several films and the mean value of these measurements was used in the calculations. A decrease of the lumen by more than 30% of the cross-section area was denoted "stenosis" A corresponding decrease of less than 30 % of this area, or irregularity in the tracheal wall, was denoted "irregularity".

Radiography of the larynx was performed when stricturing lesions were observed on inspection. Tomography was generally used.

5. *Evaluation of vocal disturbances*

At the follow-up examination the patient was usually asked whether hoarseness or other vocal changes had occurred after the period of intubation, and if so the duration of these symptoms. The author evaluated the voice at this examination and at the repeated examinations of the patients in group F_2. If the patient considered that his voice was normal and the author noted no vocal change, this was denoted "normal".

If the patient considered that he was slightly hoarse, that he had phonasthenia or that his singing voice had deteriorated, or at the follow-up examination the author detected slight hoarseness, this was noted as "slightly hoarse". Finally, patients with unequivocal hoarseness were classified as "hoarse".

6. *Methods of post mortem studies*

The laryngotracheal preparations were fixed in 10% neutral formalin. After fixation, the preparations were cut along the ventral midline, after which the larynges were opened out for photographing and for recording the extent of mucosal changes produced by the intubation. After the preparations had been photographed, each one was divided into two halves by cutting along the midline in the posterior wall of the larynx and trachea. Pieces were then cut out of each half at different levels, as shown in Fig. 9.

When considered necessary, some of these pieces were then taken for decalcification during 1–4 days (in equal parts of 44% formic acid and 20%

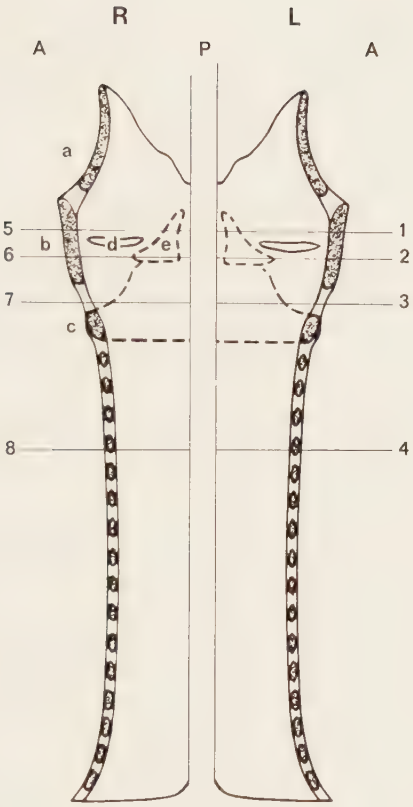


FIG. 9.—Schematic drawing of laryngotracheal specimen, split along the posterior (P) and anterior (A) midline. a. Epiglottis; b. Thyroid cartilage; c. Cricoid cartilage; d. Sinus of Morgagni; e. Arytenoid cartilage. Sections for microscopic examination were taken from 4 levels (1–4) of the left (L) half and 4 levels (5–8) of the right (R) half of the specimen.

sodium citrate with pH 1.9). Further histological preparation and staining (using the picric acid method of VAN GIESON and hematoxylin eosin) were performed according to the current methods.

Microscopic examination of the preparations and recording of the histopathological findings were carried out for each level and either side with respect to inflammation, necrosis and ulceration. The depth of these changes was determined according to the following scheme:

Inflammation:

1. No visible changes.
2. Comprising the epithelium and the lamina propria.
3. As in (2) and with extension into the submucosal layer but with intact perichondrium.
4. Comprising the mucosa, the submucosal layer and the perichondrium or cartilage.

Necrosis:

As above.

Ulceration:

1. No visible changes.
2. Comprising superficial (= erosion) epithelial defect with intact lamina propria.
3. Comprising the lamina propria and in some cases the submucosal layer but with intact perichondrium.
4. Comprising the mucosa and submucosal layer with penetration of the perichondrium.

Ulceration and necrosis were listed separately. When ulceration continued in the form of necrosis, the latter was noted only if it was considerably deeper than the ulceration.

Since the construction of the mucosa varies in different parts of the larynx and trachea this must also be taken into consideration when the laryngo-tracheal damage is being evaluated.

Chapter IV

COMPLICATIONS OCCURRING DURING THE PERIOD OF ENDOTRACHEAL INTUBATION

In this investigation all patients in the post mortem series (79 cases) and the follow-up series (312 cases) were studied.

A. *Obstructed airway*

1. *Adults*

No severe obstruction in the endotracheal tube or caused by the tube occurred in any of the adult patients. Changing of the tube was seldom required for the reason of inspissated secretions in the tube, and when this was necessary there was never any acute emergency.

Obstruction of the passage to the left lung due to the fact that the endotracheal tube had been inserted too far into the respiratory tract occurred primarily in isolated cases, but since chest radiography was performed routinely, the position of the tube could be checked and any necessary correction carried out. No case of accidental dislocation of the endotracheal tube occurred.

2. *Infants and children*

As in adults, in some cases the endotracheal tube entered the right main bronchus on intubation. It was always possible to correct this without any serious complications occurring.

One serious threat to life occurred as a result of accumulation of secretions in the endotracheal tube (case C23).

This was a boy who at the age of one month underwent operation for transposition of the aorta and pulmonary artery. During the operation he had repeated cardiac arrest. Postoperatively he was in a relatively poor condition and was treated with a respirator via an endotracheal tube. On the fifth day after the operation he had acute respiratory arrest due to accumulation of secretions in the endotracheal tube, resulting in cardiac arrest, which was relieved within 2–3 minutes by external cardiac massage. After this his venti-

lation was satisfactory and his circulation adequate, taking into consideration the pathologically changed circulatory conditions which were already present. Respirator treatment was given for a further 16 days, after which the endotracheal tube was removed. On examination of the larynx at the time of extubation, moderate oedema was observed in the arytenoid region. There was general erythema in the larynx, and a minor mucosal defect was observed on the right vocal cord within the medial part of the vocal process (Plate V: 22a, b; p. 123). No symptoms of obstruction in the upper airway occurred after extubation, and at follow-up examination 5 months later the state of the larynx and the voice were normal. Subsequently this patient has shown symptoms of a cerebral lesion, with spasticity and mental retardation.

As in the adult patients, chest radiography was performed routinely after intubation, and especially in cases where the clinical findings were uncertain this made it possible to check the position of the tube and correct it if necessary. No cases of accidental dislocation of the endotracheal tube occurred.

3. *Discussion*

Stagnation of secretions in the endotracheal tube has sometimes caused problems when fine-calibre tubes have been used. In those patients of the present series for whom ultrasonic nebulizers were available, however, essentially no such problems arose. Other authors have described severe complications in children, some of them with a fatal outcome, caused by obstruction by inspissated secretions in the tube (Aberdeen and Glover, 1967, Striker *et al.*, 1967, Abbott, 1968). Striker *et al.* reported that "hourly instillation of 1.0 to 2.0 ml of sterile saline solution into the tube was followed by aseptic endotracheal aspiration", but neither this author nor the others mentioned stated whether air humidifiers were used continuously in those cases where these complications occurred.

In case C23 described above, only the standard humidifying unit of the respirator was used. Whether the cerebral lesion which later became manifest in this boy was of prenatal, perinatal or postnatal origin cannot be decided. If it was acquired postnatally, it is still extremely difficult to determine whether it occurred as a result of the circulatory collapses during the operation or following the cardiac arrest in the postoperative period.

The fact that in no case was the endotracheal tube accidentally dislocated may be attributed to the extreme care taken with fixation of the tube, and to the continuous supervision of the patient. The risk of accidental extubation (Aberdeen and Glover, 1967) or aspiration of the endotracheal tube (Striker *et al.*, 1967) in children would seem to be negligible if tubes of the Jackson Rees type are used and if fixation of the tube is performed in principle according to the recommendations of Jackson Rees and Owen-Thomas (1966).

Routine chest radiography after intubation and during the intubation period have been found to be valuable for checking the position of the tube and the lung status, and have contributed to the prevention of complications.

B. *Changes in pulmonary parenchyma observed on repeated radiographs during the period of endotracheal intubation*

1. *Adults*

As shown in Table 11, in the follow-up series 48% of the patients showed normal chest radiographs during the intubation period. In 31%, initially observed parenchymal changes did not alter, in 11% there was a progression

Table 11.

Repeated chest radiography during the period of endotracheal intubation in adult patients in the follow-up series.

Chest radiography	Thoracic surgery	General surgery	Drug poisoning	Miscell-aneous	No. of patients
Normal	98	6	15	8	127 (48%)
Unchanged	65	3	4	9	81 (31%)
Progression	23	1	2	3	29 (11%)
Regression	16	1	3	3	23 (9%)
Variable	1	–	1	–	2 (1%)
Not performed	–	–	4	1	5
No. of patients	203	11	29	24	267

and in 8% a regression of such changes, and in 1% the lung picture varied.

The findings in the adult patients in the post mortem series are presented in Table 12. In 38% of the investigated cases in this series the pulmonary parenchyma was normal. In 22%, initially observed parenchymal changes were unaltered, in 22% they had progressed and in 14% they had regressed.

Table 12.

Repeated chest radiography during the period of endotracheal intubation in adult patients in the post mortem series.

Chest radiography	Thoracic surgery	General surgery	Drug poisoning	Miscell-aneous	No. of patients
Normal	2	7	1	11	21 (38%)
Unchanged	1	3	–	8	12 (22%)
Progression	2	5	1	4	12 (22%)
Regression	1	4	–	3	8 (14%)
Variable	–	1	–	1	2 (4%)
Not performed	–	7	–	5	12
No. of patients	6	27	2	32	67

Table 13.

Repeated chest radiography during the period of endotracheal intubation in infants and children in the follow-up series.

Chest radiography	Age		No. of patients
	< 1 year	≥ 1 year	
Normal	5	11	16 (36%)
Unchanged	3	5	8 (18%)
Progression	1	5	6 (13%)
Regression	7	3	10 (22%)
Variable	4	1	5 (11%)
Not performed	–	–	–
No. of patients	20	25	45

2. *Infants and children*

Tables 13 and 14 give the results of chest radiography in children. The parenchymal changes decreased during the intubation period in a relatively large number of children below the age of 1 year. In the follow-up series, normal pulmonary parenchyma was found in 36% of the children. Initially observed parenchymal changes remained unaltered in 18%. In 13% such changes progressed, and in 22% they regressed.

In 5 infants and children of the post mortem series the information available was incomplete, and the series was too small for evaluation.

Table 14.

Repeated chest radiography during the period of endotracheal intubation in infants and children in the post mortem series.

Chest radiography	Age		No. of patients
	< 1 year	≥ 1 year	
Normal	2	1	3 (43%)
Unchanged	1	–	1 (14%)
Progression	–	–	– (0%)
Regression	–	–	– (0%)
Variable	3	–	3 (43%)
Not performed	3	2	5
No. of patients	9	3	12

3. *Discussion*

The aim of the comparisons which were made of the condition of the pulmonary parenchyma by means of repeated chest X-rays was to obtain an idea of how the parenchyma behaved during the intubation period. Atelectasis sometimes occurs as a result of inspissated secretions and inadequate ventilation, and difficulties in keeping the respiratory tract free from accumulated secretions on prolonged endotracheal intubation have been encountered (Brandstater, 1962, Tonkin and Harrison, 1966, Weg, 1967).

Apart from the fact that it can cause acute respiratory arrest, inspissation of secretions in the bronchial tree should also be manifested in atelectatic changes during the intubation period.

Parenchymal changes were observed initially in more than half of the patients. This is in accordance with the composition of the series, in which the majority of patients had been subjected to thoracic surgical operations and where other patients, including infants, had been intubated initially and treated with a respirator for reasons of extensive pneumonia or other diseases affecting the pulmonary parenchyma.

Inspissation of secretions during prolonged endotracheal intubation probably only in exceptional cases gave rise to atelectasis or other parenchymal changes. This is supported especially by the finding of a regression of the lung changes in 7 out of 15 children below the age of 1 year in the follow-up series. In this group there was only 1 patient in whom a progression was observed. If, due to difficulties in sucking the airways free, inspissated secretions were to give rise to lung changes of the atelectatic type, this should have been just in this category, where fine-calibre tubes were used.

In adult patients the incidence of both "regression" and "progression" was higher in the post mortem series than in the follow-up series. This is in accordance with the finding that at the time of intubation, parenchymal changes were more often already present in the former group. The basic disease could not be arrested, however, despite the fact that in many cases the air content of the pulmonary parenchyma increased considerably as a sign of improved ventilation during the intubation period.

Chapter V

ACUTE DAMAGE IN THE LARYNX AND TRACHEA FOLLOWING PROLONGED ENDOTRACHEAL INTUBATION AND ITS HEALING COURSE

A. *Location and extent of postintubation damage in the larynx and trachea*

1. *Adults*

Mucosal changes within relatively constant regions were observed without exception after prolonged endotracheal intubation. These were located on the medial side of the arytenoid cartilages, for the most part on the vocal process, in the interarytenoid region and in the inner posterior lateral areas of the cricoid cartilage (Fig. 16; p. 82).

Circumferential mucosal changes were sometimes seen in the trachea where the inflated cuff had been located (Fig. 17) and in exceptional cases at the level of the cricoid ring (Plate I: 4; p. 115), at the level of the vocal cords and in the subglottic space close to them (Plate I: 5a).

The depth of the lesions varied from a superficial epithelial abrasion with a slight inflammatory reaction to deep mucosal ulceration surrounded by pronounced inflammation.

2. *Infants and children*

The mucosal changes observed in the respiratory tract in infants and children were less pronounced than in adults, but some form of reaction was seen in all children after prolonged endotracheal intubation. Especially infants below the age of 1 year tolerated the endotracheal tube well and they usually reacted only with moderate hyperaemia and/or slight oedema, generally in the laryngeal mucosa (Plate V: 21 and 23). However, small local mucosal defects were sometimes observed in these patients also (Plate V: 22b and 24a), and in 2 patients (cases C2 and C20) circumferential mucosal necrosis occurred at the level of the cricoid ring; in another patient (case C3), deep ulceration was seen on the medial side of the arytenoid cartilages and within the interarytenoid area. No localized changes in the trachea were observed in infants or children after prolonged endotracheal intubation.

B. *Classification of postintubation damage in the larynx and trachea*

Acute reactions in the larynx and trachea were studied during the first half of this investigation with regard to location and extent. On the basis of the experiences obtained, a classification was made of the acute postintubation damage in the patients in group F_1. In this classification, consideration was taken of both the circumferential extent and the depth of the mucosal damage, as follows:

I. Hyperaemia or oedema without macroscopic ulceration.
II. Continuous superficial ulceration of the mucous membrane comprising less than $\frac{1}{3}$ of the circumference of the airway.
III. Continuous deep ulceration of the mucous membrane along less than $\frac{1}{3}$ of the circumference of the airway, or continuous superficial ulceration comprising more than $\frac{1}{3}$ of the circumference of the airway.
IV. Deep ulceration of the mucous membrane with exposed cartilage, or continuous deep ulceration comprising more than $\frac{1}{3}$ of the circumference of the airway.

Plate I: 1, 2 and 3 illustrates damage which was classified into grades I, II and III, respectively. The damage shown in Plate I: 6a was also classified as grade III. In this case (where a Magill red rubber tube was used), the tissue reaction around the necrosis was found to be more active, with greater oedema around the lesion. Plate I: 7a was taken 24 hours after extubation. In this case greater deposition of fibrin had had time to occur. The damage was classified as grade II.

The mucosal reactions illustrated in Plate I: 4 and 5a were assessed as superficial mucosal damage with circumferential distribution, and were classified as damage of grade III. There was no possibility of photographing damage of grade IV in the acute stage.

Table 15 summarizes the results of the assessment made according to the above principles. Damage of grade II (58%) predominated in the total series, and damage of grade IV occurred in only 4 cases (2%). Damage of grades I

Table 15.

Classified acute damage in the larynx and trachea following prolonged endotracheal intubation in 125 adult patients and 36 infants and children (Group F_1).

Grade of damage	Adults		Infants and children		No. of patients
	Men	Women	< 1 year	≥ 1 year	
I.....	8 (13%)	10 (15%)	12 (75%)	5 (25%)	35 (22%)
II.....	38 (63%)	40 (61%)	3 (19%)	12 (60%)	93 (58%)
III.....	13 (22%)	14 (22%)	1 (6%)	1 (5%)	29 (18%)
IV.....	1 (2%)	1 (2%)	–	2 (10%)	4 (2%)
No. of patients.	60(100%)	65(100%)	16(100%)	20(100%)	161(100%)

TABLE 16.

The patency of the upper airway immediately after prolonged endotracheal intubation, and reasons for secondary tracheostomy in adult patients in the follow-up series.

Patency of upper airway and reasons for secondary tracheostomy	Thoracic surgery	General surgery	Drug poisoning	Miscell-aneous	No. of patients
Free respiration after extubation.....	172	7	24	16	219 (82%)
Respiratory obstruction after extubation managed without tracheostomy....	1	–	–	1	2 (1%)
Respiratory obstruction after extubation necessitating tracheostomy.....	–	1	3	–	4 (1%)
Tracheostomy because of expected long term respirator treatment.....	30	3	2	7	42 (16%)
No. of patients.....	203	11	29	24	267(100%)

and III was considered to have occurred in essentially equal frequencies (22% and 18%, respectively).

In adults and children, the major part of the damage was of grade II. In infants, on the other hand, grade I predominated (75%).

C. *The patency of the upper airway following prolonged endotracheal intubation and indications for secondary tracheostomy*

1. *Adults*

Table 16 gives the clinical respiratory conditions immediately after extubation, with regard to the patency of the upper airway, and also the reasons for secondary tracheostomies. In 219 patients the airway was assessed as free. Expected prolonged respirator treatment comprised the indication for tracheostomy in 42 adult patients in the follow-up series (see also table 9).

Respiratory obstruction occurred in 6 adult patients in the same series, and the causes are given below.

Circumferential subglottic swelling with stridor was observed in 1 patient (case 226, Plate I: 4), necessitating intensified conservative therapy. In 2 patients the swelling (cases 235 and 318, Plate I: 5a) led to tracheostomy.

Extensive *necrosis within the inner posterior parts of the larynx* was observed in 1 patient with respiratory obstruction (case 287). In the acute stage the necrosis was accompanied by oedema and slough formation, which necessitated tracheostomy.

Circumferential mucosal damage in the trachea, 3–4 cm in length and resulting in respiratory obstruction occurred in 2 patients (cases 241 and 248). The damage consisted of superficial mucosal necrosis accompanied by oedema and inspissation of secretions, which in one of the patients necessitated tracheoscopy and suctioning, and in the other tracheostomy.

TABLE 17.

The patency of the upper airway immediately after prolonged endotracheal intubation and reasons for secondary tracheostomy in infants and children in the follow-up series.

Patency of upper airway and reason for secondary tracheostomy	Age		No. of patients
	< 1 year	≥ 1 year	
Free respiration after extubation.....	16	17	33 (73%)
Respiratory obstruction after extubation managed without tracheostomy.....	–	–	–
Respiratory obstruction after extubation necessitating tracheostomy.....	1	4	5 (11%)
Tracheostomy because of expected long term respirator treatment.....	3	4	7 (16%)
No. of patients.....	20	25	45(100%)

2. *Infants and children*

Free respiration was noted in 33, and expected prolonged respirator treatment was the reason for secondary tracheostomy in 7 infants and children in the follow-up series. Respiratory obstruction following prolonged endotracheal intubation occurred proportionally more often than in adult patients (Table 17). Children over 1 year of age were especially affected by respiratory difficulties necessitating tracheostomy (see also table 9).

Respiratory obstruction occurred in 5 infants and children after extubation, and this necessitated tracheostomy in all cases. In 2 of these (cases C4 and C6) the respiratory obstruction was due to *subglottic oedema,* in 2 (cases C2 and C20) to *circumferential mucosal necrosis at the level of the cricoid* and in 1 (case C3) to deep *ulceration on the medial side of the arytenoid cartilages and in the interarytenoid region.*

A further few infants and children had mild symptoms of respiratory distress on exertion. At rest, however, the respiration was free and these children were therefore assigned to the group of "free respiration after extubation".

D. *Healing course of acute postintubation damage in the larynx and trachea*

1. *Different types of healing course*

a. Adults

Adult patients in group F_2 in the follow-up series were examined every 15th day ($\pm$ 7 days) until there was complete clinical regression of the intubation damage or until a stationary residual lesion was observed.

Healing courses of two main types were observed:

1. Healing with *rapid epithelialization of the lesions*—"primary healing". Plate I: 5 a, b; 6 a, b, c and 7 a, b, c all illustrate how "primary healing" took

place. All of these lesions healed within 1 month. In the 69 adult patients who were examined repeatedly, 42 (61 %) healed in this way.

2. Healing via a stage of *granuloma formation*—"secondary healing". In 26 patients (38 %), more or less pronounced granuloma formation occurred during the healing period, and in 1 patient (case 256) a cyst developed on the left vocal process (Plate III: 14 b), and this was extirpated 10 months after the period of intubation, with subsequent healing within 1 month (Plate III: 14 c).

Spontaneous successive regression of the granulomas took place in 24 patients, and healing without residual lesions after an average of 86 days (SD = 61, range 1–10 months, median value 60 days). Plate II: 8 a, b, c, d; 9 a, b, c, d, e and 10 a, b, c, all show healing courses where granulomas had developed and subsequently regressed spontaneously.

In 1 patient (case 305), a granuloma continued to grow during a period of 5 months, and began to give respiratory distress, which necessitated extirpation (Plate III: 12 a, b, c). In 1 patient (case 287), the granuloma changed to scar formation—see below.

In 25 cases the granulomas were localized to the medial side of the arytenoid cartilages, mostly on the vocal process. In one of these patients (case 309, Plate II: 8 a, b, c) granulomas were seen both on the medial side of the arytenoid cartilages and subglottically in the lateral posterior region, and in another patient (case 287, Plate IV: 15 a, b) granulation tissue alone formed in the posterior subglottic region about 5 mm below the plane of the vocal cords. In the latter case a fibrous scar formed later at the location of the granulation tissue (Plate IV: 15 c, d); the scar was about 2–3 mm broad and equally high, and extended along just over $\frac{1}{3}$ of the circumference of the airway at this level. The scar tissue was extirpated 6 months after the period of intubation (Plate IV: 15 d), because of phonasthenia. After the operation the patient noted a marked improvement, and the result has since remained good even though the slightly raised scar tissue re-formed to some extent. (Plate IV: 15e).

In the remaining adult patients in the follow-up series (i.e. excluding group F_2) there were 5 further patients with postintubation granulomas which gave such symptoms that extirpation was performed before the patients were called for the follow-up examination (cases 13, 50, 87, 192 and 202). As a rule the symptoms were mild and consisted of an irritative cough, hoarseness and transient sensations of suffocation. Extirpation of these granulomas was performed 2–6½ months after the period of intubation. In 3 patients the granulomas were bilateral, in 1 patient on the right side only and in 1 patient on the left side only. In the latter patient the granuloma was localized within the anterior half of the vocal cord, and in the others on the medial side of the arytenoid cartilages. In one case the granuloma recurred twice and was reextirpated.

One further granuloma was discovered at the follow-up examination (case 190, Plate IV: 17). This was localized subglottically, to the left, and had given

no symptoms for 13½ months. It was extirpated and healing took place within 1 month.

The healing times for adult patients in group F_2 are shown in Fig. 10. The mean value was 56 days (SD = 63; range 15 days to 11 months; median value 30 days).

The classified acute damage in the larynx and trachea and the healing times are given in Table 18.

High grade acute damage shows good correlation to a long healing time.

b. Infants and children

Infants and children in group F_2 in the follow-up series were examined, as in the case of adults, every 15th day (± 7 days) until the damage was healed

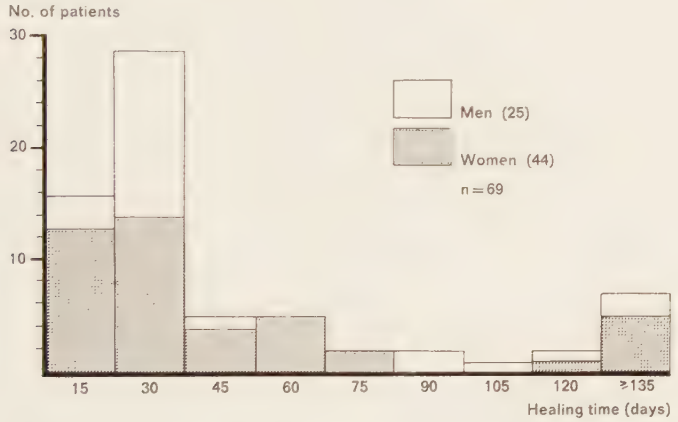


Fig. 10.—Healing time for acute postintubation damage in adult patients of group F_2 in the follow-up series.

Table 18.

Initial classification of acute damage in the larynx and trachea following prolonged endotracheal intubation and healing time in adult patients (Group F_2).

Healing time (days)	Grade of damage				No. of patients
	I	II	III	IV	
≤30	7	34	4	–	45
31–60	–	6	4	–	10
61–90	–	3	–	1	4
≥91	–	2	7	1	10
No. of patients	7	45	15	2	69

or until a stationary residual lesion was observed. They were also examined 7 days after the end of the intubation period.

The healing course differed from that of the adults in that no granuloma formation was observed. As a rule, redness and any swelling regressed within a few days, and most lesions which occurred healed rapidly. Altogether 31 infants and children were followed up with repeated examinations. Of these, 14 returned to normal within 7 days, 13 within 15 days and 1 within 30 days.

Fibrous scar formation occurred in the remaining 3, who had a prolonged healing course.

Circumferential fibrous stenosis at the level of the cricoid developed in 2 patients (cases C2 and C20; see pp. 52 and 55) as a result of circumferential mucosal necrosis at this level. The healing course for the most pronounced of these lesions (case C20) is illustrated in a series of photographs (Plate V: 25 a, b, c, d). In this case the subglottic necrosis developed, within about 1 month, into a rigid stenosis with a lumen of about 2 mm diameter (Plate V: 25 a). Bougienage was performed on 3 occasions during the early stage. The stenosis gradually regressed and after a tracheostomy period of 4½ months the cannula could be removed (Plate V: 25 c), after which no respiratory or vocal symptoms occurred. Case C2 showed a similar course but in this case the stenosis was less pronounced and good spontaneous regression took place during a tracheostomy period of 5 months.

In 1 child (case C3) who sustained extensive mucosal damage on the medial side of the arytenoid cartilages (see pp. 52 and 55) and within the inner posterior parts of the larynx at the same level, a fibrous scar developed, starting at the left vocal process and bridging the left part of the interarytenoid space (Plate V 26: a, b).

The classified acute damage and the healing times are given in Table 19.

Only 3 infants and children had acute damage classified as grades III and IV and extended healing times with fibrous scarring in the larynx.

Table 19.

Initial classification of damage in the larynx and trachea following prolonged endotracheal intubation and healing times in infants and children (Group F_2).

Healing time (days)	Grade of damage				No. of patients
	I	II	III	IV	
≤ 7	13	1	–	–	14
8–15	1	12	–	–	13
16–30	–	1	–	–	1
≥31	–	–	1	2	3
No. of patients	14	14	1	2	31

TABLE 20.

Period of vocal disturbances following prolonged endotracheal intubation in adult patients in the follow-up series.

Voice	Thoracic surgery	General surgery	Drug poisoning	Miscellaneous	No. of patients
Prolonged endotracheal intubation only					
Voice after extubation					
Normal (Slightly hoarse < 1 week)	99	5	7	8	119 (55%)
Hoarse 1 week	18	–	3	2	23 (11%)
Hoarse 2 weeks	22 (87%)	– (71%)	7 (75%)	– (69%)	29 (13%)
Hoarse 3 weeks	5	–	1	1	7 (3%)
Hoarse 4 weeks	4	–	–	–	4 (2%)
Hoarse > 4 weeks	23 (13%)	2 (29%)	6 (25%)	5 (31%)	36 (16%)
Not recorded	2	–	–	1	3
Secondary tracheostomy performed Decannulation within 4 weeks					
Voice after decannulation					
Normal (Slightly hoarse < 1 week)	18	3	1	2	24 (59%)
Hoarse 1 week	3	–	–	–	3 (7%)
Hoarse 2 weeks	1	1	1	–	3 (7%)
Hoarse 3 weeks	2	–	–	–	2 (5%)
Hoarse 4 weeks	1	–	–	–	1 (2%)
Hoarse > 4 weeks	5	–	2	1	8 (20%)
Not recorded	–	–	1	1	2
Tracheostomy cannula in situ ≥ 4 weeks					
	–	–	–	3	3

2. *Period of vocal disturbances following prolonged endotracheal intubation*

a. Adults

The duration of the vocal disturbances following the period of intubation in adult patients in the follow-up series is given in Table 20. The patients have also been divided into different indication groups. For patients who underwent secondary tracheostomy and were decannulated within 1 month, the duration of the vocal disturbances which followed the decannulation is also given in Table 20. Three patients had a tracheal cannula for more than 1 month, and the voice could not therefore be assessed in these patients.

221 patients were treated by prolonged endotracheal intubation alone. For 3 of these no information on the vocal condition could be obtained. Of the remaining 218 patients, the voice became normal in less than 1 week in 119, in 1 week in 23, in 2 weeks in 29, in 3 weeks in 7 and in 4 weeks in 4. In 36 patients vocal disturbances persisted for longer than 1 month.

Patients treated by both prolonged endotracheal intubation and secondary tracheostomy had, on the whole, equally long durations of vocal disturbances after decannulation as patients treated by prolonged intubation alone had after extubation (Table 20).

b. Infants and children

The duration of the vocal disturbances after the period of intubation in infants and children in the follow-up series is shown in Table 21. Infants and children are listed separately. As in the case of adults, for the children who underwent secondary tracheostomy and were decannulated within 1 month, the duration of the vocal disturbances following decannulation is given in Table 21. Five infants and children had a tracheal cannula for longer than 1 month, and the voice could not therefore be assessed in these patients.

TABLE 21.

Period of vocal disturbances following prolonged endotracheal intubation in infants and children in the follow-up series.

Voice	Age		No. of patients
	< 1 year	≥ 1 year	
Prolonged endotracheal intubation only			
Voice after extubation			
Normal (Slightly hoarse < 1 week)	10	9	19 (60%)
Hoarse 1 week	2	5	7 (22%)
Hoarse 2 weeks	1	1	2 (6%)
Hoarse 3 weeks	2	–	2 (6%)
Hoarse 4 weeks	–	2	2 (6%)
Hoarse > 4 weeks	–	–	– (0%)
Not recorded	1	–	1
Secondary tracheostomy performed *Decannulation within 4 weeks*			
Voice after decannulation			
Normal (Slightly hoarse < 1 week)	–	1	1 (14%)
Hoarse 1 week	–	2	2 (29%)
Hoarse 2 weeks	–	1	1 (14%)
Hoarse 3 weeks	–	–	– (0%)
Hoarse 4 weeks	–	–	– (0%)
Hoarse > 4 weeks	1	1	2 (29%)
Not recorded	–	1	1
Tracheostomy cannula in situ ≥ 4 weeks	3	2	5

33 infants and children were treated by prolonged endotracheal intubation alone. For 1 infant no information on the vocal condition could be obtained. Of the remaining 32 patients, the voice became normal in less than 1 week in 19, in 1 week in 7, in 2 weeks in 2, in 3 weeks in 2 and in 4 weeks in 2. No infants or children in this group had vocal disturbances for longer than 1 month.

E. *Discussion*

ad A. The cause of the described localization of the damage after prolonged endotracheal intubation is to be found in the discrepancy between anatomical conditions within the upper airway and either the shape of the endotracheal tube (Dwyer *et al.*, 1949, Barth and Meyer, 1962, Bergström *et al.*, 1962, Kowalski, 1960, Lindholm, 1968) or its width (Nilsson, 1951, Dam and Zwergius, 1952, Holmdahl and Lindholm, 1967, Lindholm, 1967, 1968, Stocks, 1968).

Further, the motor activity of the vocal cords (Jackson, 1953) probably plays an important role in the occurrence of damage specifically on the vocal process, which has a thin mucoperichondrium (Stein *et al.*, 1960, Jackson, 1953). The inflated cuff of the endotracheal tube or a tracheal cannula involves a risk of circumferential damage in the trachea (Stiles, 1965, Gibson, 1967, Bryce *et al.*, 1968 Lindholm, 1968, Carroll *et al.*, 1969).

The extent and, especially, the depth of the lesions may also be influenced by movements between the larynx and the endotracheal tube, by the nature of the tube surface and the biological properties of the material, or by residual products from sterilization procedures (Mallette and von Haam, 1952, Little and Parkhouse, 1962, Guess and Stetson, 1968, Harrison and Tonkin, 1968, Rendell-Baker, 1968, Stetson, 1968). Increased vulnerability of the mucosa resulting from poor circulation, infection etc. can also be expected to be of importance in this respect.

The length of the intubation period has been considered by many authors (Nilsson, 1951, Dam and Zwergius, 1952, Bergström, 1962, Elbrønd, 1964) to be of greater importance than any other factor for the occurrence of damage in prolonged endotracheal intubation. There is no doubt that this duration is of considerable significance in this respect. However, the localization, extent and depth of the damage would seem to be a product of time and the mechanical, chemical and physical influence to which the larynx is subjected by the endotracheal tube.

ad B. Classification of damage after endotracheal intubation has been carried out by means of a score system in post mortem studies by Hedden *et al.* (1969). According to a special system, these authors have assessed the lesions with respect to "submucosal hemorrhage, oedema, inflammation and ulceration" and also with respect to the superficial extent and the depth of the lesions within different areas.

For clinical assessment, a somewhat simpler classification of the lesions would seem preferable. In such a classification the most important aim would seem to be an assessment of the acute damage with regard to its importance for the occurrence of irreversible changes. In the studies which preceded the classification used in this investigation, consideration was taken of both this question and the difficulties which existed on evaluation of certain criteria. Thus the longitudinal extent of the mucosal reaction in the airway was difficult to establish with the technique used. Experience has indicated, however, that the extent of the lesion in this direction plays a smaller part than that along the circumference of the airway, and this was more easily assessed. The depth of the ulceration or necrosis probably plays a large role in the healing course. The former is relatively easily assessed immediately after extubation, but is more difficult even after only a few hours, when fibrin deposits and membrane development mask the damaged area. In the classification made here the lesions were grouped with respect to estimated depth and extent.

The results of the classification of the acute damage observed after prolonged endotracheal intubation in this series are presented in Table 15. It is difficult

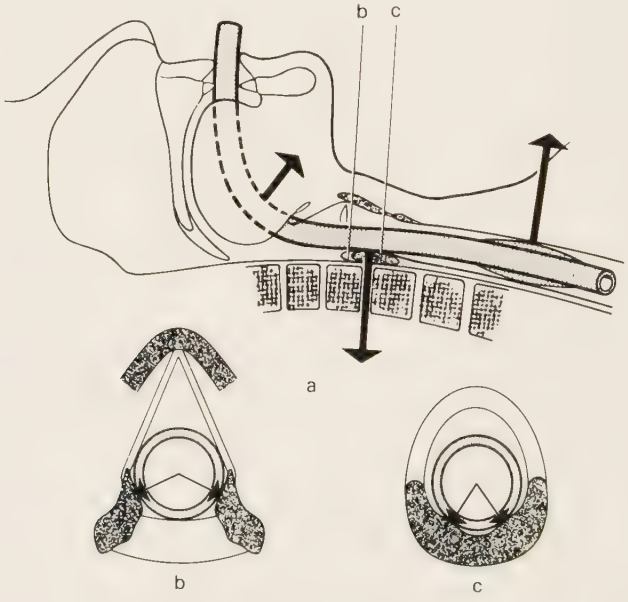


FIG. 11.—Schematic drawing showing an endotracheal tube *in situ* in a patient.

a. The arrows show the direction of the forces being exerted by a straight or slightly arched endotracheal tube owing to its elasticity, in an attempt to regain its original shape.

b. Cross-section through the larynx at the vocal cord level. Forces are exerted against the medial sides of the arytenoid cartilages.

c. Cross-section through the larynx at the level of the middle of the cricoid cartilage. Forces are exerted on the contact surfaces in the postero-lateral areas.

to compare these with results from other investigations, since there has been no uniform method of classification.

ad C. An assessment of acute postintubation damage which has been of such an extent as to necessitate tracheostomy will give a good idea of the mechanical conditions which can contribute to damage on prolonged endotracheal intubation. These lesions vary in type and nature, and in the following will be discussed with respect to their aetiology.

Deep ulceration in the posterior parts of the larynx in 1 adult female (case 287) and in 1 boy (case C3) was considered to have arisen partly as a result of the unfavourable shape of the endotracheal tube. Fig. 11 illustrates schematically the areas which were subjected to pressure during intubation with a conventional straight or slightly bent endotracheal tube. The strength which is needed to reshape the tube according to the anatomy of the upper airway is generally considerable. Barth and Meyer (1962) state that a Magill tube (40 Charrière) exerts a pressure, with its tip against the anterior wall of the trachea, of between 126 and 350 g depending upon the curvature radius of the tube and position of the head.

The posterior parts of the larynx interposed between the cervical vertebrae and the tube act as a fulcrum. The tongue usually falls backwards towards the throat in unconscious patients and exerts pressure from the ventral side on to the oral part of the tube. This contributes to making the pressure which is produced by the tube against the posterior part of the larynx considerably greater than that which is exerted against the anterior wall of the trachea. Tubes of PVC and reinforced latex have the same disadvantage as tubes of red rubber, even though considerably less strength is required to reshape the two former types.

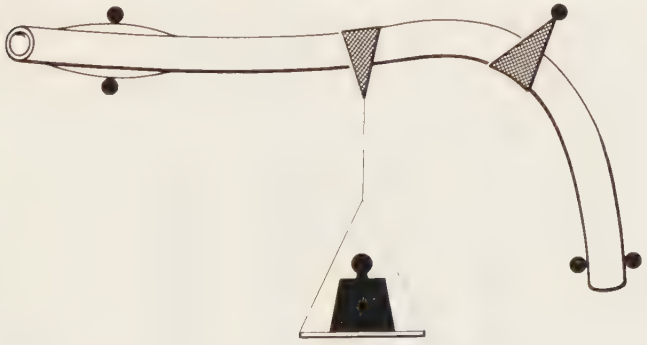


Fig. 12.—Model experiment to determine roughly the force which is exerted against the dorsal side of the larynx when a straight or slightly arched endotracheal tube is reshaped according to the patient's airway. It is assumed that the patient has been intubated orally and his head is held in a normal position.

In a simple model experiment illustrated in Fig. 12 determinations were made of the strength required to reshape tubes of different manufacture to a form which resembles the airway seen from the side. The experiment was performed at a temperature of 35° C, and tubes with the same internal diameter (7.5 mm) were used. The strength which was exerted in a dorsal direction in the larynx was determined.

For the Magill red rubber tube (Franklin), 475 g was required for it to assume the desired shape, while 70 g was sufficient to reshape the BOC reinforced latex tube and 175g to reshape the Flotex reinforced latex tube and the Portex PVC tube.

Tubes of smaller diameter and thinner walls require considerably less reshaping strength than larger tubes, and it can be expected thus that damage caused by their unfavourable shape will be smaller. This is also in agreement with the fact that reactions of the type which are caused by reshaping pressure of the tube were considerably smaller in the youngest children than in the adults.

Tubes which follow the anatomical shape of the airway when the head of the patient is bent backwards have been constructed previously (Dwyer *et al.*, 1949, Kuhn, 1964, Droh, 1965, Tashayod, 1967). In this position the pressure of a conventionally shaped tube will be greatest (Barth, 1952). In prolonged endotracheal intubation it is desirable that the patient lies with the head in a normal position, and the tubes mentioned then do not fit satisfactorily. The author has therefore designed a tube which follows the airway in an anatomically correct manner under these conditions (Lindholm, 1967, 1968). The tube is manufactured by PVC (Portex)[1]) and is shown in Fig. 13.

[1]) Portex Ltd., Hythe, Kent, England.

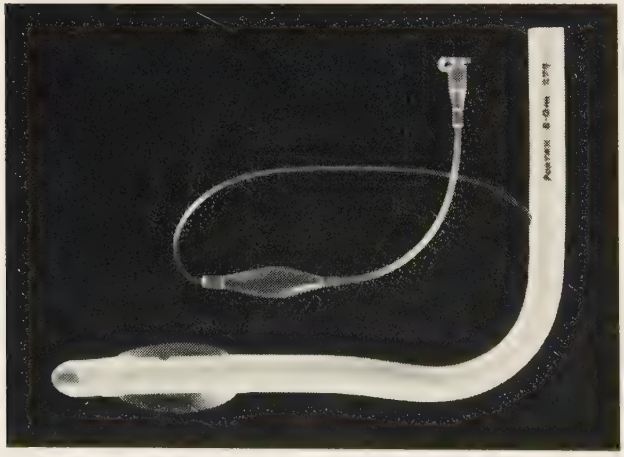


Fig. 13.—The orotracheal tube designed by the author for prolonged intubation.

A subglottic reaction which necessitated tracheostomy was considered to have been caused by a tube too wide in relation to the lumen of the larynx in 4 children (cases C2, C4, C6 and C20) and 1 adult (case 318) in this series. There were distinct clinical signs in these cases that a tube with too large an external diameter had been used. These observations are also supported on studying the size of the tube used in relation to age in surviving children (Fig. 6). It is found that those children below the age of 10 years who had reacted in the above described manner had had the largest tubes in their age group. Children between 10 and 16 years of age do not follow this rule, but since puberty occurs at different ages and the larynx in this category can thus be expected to vary considerably in size, this does not contradict the clinical observations.

The subglottic reaction was interpreted as circumferential mucosal necrosis in 2 children (cases C2 and C20), and in the remaining cases subglottic oedema was observed. None of the 25 surviving children who were the last of the series to undergo prolonged endotracheal intubation needed tracheostomy because of laryngotracheal complications, and neither did they have any respiratory obstruction in the postintubation course.

The cricoid cartilage is the only complete cartilage ring in the upper respiratory tract. This means that it is this cartilage that constitutes the absolute limitation of the lumen. If a tube with an external diameter exceeding the diameter of the lumen is used, the mucosa will be compressed by the tube. In mild cases oedema occurs in the lateral part of the subglottic space or as a circular swelling in the loose subglottic tissue (Holinger and Johnston, 1960). These conditions are usually reversible and have also been described after short-term anaesthesia (Crispell and Hampton, 1950, Haines and Powell, 1955, and others). In more severe cases, on the other hand, an ischaemic circumferential necrosis can occur, with cicatricial stenosis as a result (Mc Donald and Stocks, 1965, Holmdahl and Lindholm, 1967, and others). Way and Sooy (1965) have shown in monkeys that oversized tubes give mucosal ulceration at the cricoid level after only 2 hours of intubation.

Lesions on the medial side of the arytenoid cartilage and the part played by the motor activity of the larynx in the occurrence of such lesions are illustrated well in 2 extreme cases (case 189, Plate III: 11 and case C3, Plate V: 26), where the effect of very little and of excessive laryngeal motor activity can be studied.

The movements which the arytenoid cartilages normally carry out automatically at each respiratory cycle, and at every cough or attempt at phonation traumatize especially the medial side of the vocal process when an endotracheal tube is interposed between these cartilages (Jackson, 1953).

Apart from the fact that trauma of "the hammer and anvil type" (Jackson, 1953) occurs on the vocal process, continuous pressure can be exerted within the same area due to tonus in the internal laryngeal muscles, or by overextension of these muscles caused by an oversized tube (Fig. 11 b).

Tonkin and Harrison (1966) compared dimensions of the larynx in men and women with the external diameter of the endotracheal tubes used. These authors found a higher frequency of damage in women and considered that a plausible explanation for this may be that larger tubes in relation to the dimensions of the larynx were used for women than for men.

Within *the middle parts of the trachea* swelling combined with superficial mucosal damage, accumulation of fibrin and accumulation of secretions gave rise to respiratory obstruction necessitating tracheostomy in one patient (case 241).

In this patient, a woman, a Portex tube with an external diameter as large as 12.4 mm had been used. When a larger tube is used, the diameter of a cuff filled to the residual volume will be correspondingly increased. The elastic properties of PVC are such that an increase of the volume in the cuff over and above the residual volume requires a large increase in pressure. It is thus not possible to determine what pressure is exerted against the tracheal wall by measuring the pressure in the inflation tube if the cuff is inflated above its residual volume. When "normal sized" tubes of PVC (7.5 mm internal diameter, 10.92 mm external diameter) are used in women, a relatively high cuff pressure is usually required for the cuff to expand sufficiently to produce a "no leak ventilation". If, with a larger tube, the same volume of air is used to inflate the cuff or if it is inflated to the pressure which is usually required normally, this results in an abnormal pressure against the tracheal wall, assuming the calibre of the trachea to be the same.

The mechanism for the occurrence of the cuff damage described here would seem to be that mentioned above, and this stresses the importance of inflating a cuff only to a sufficient extent as to prevent appreciable leakage at the insufflation pressure in question and of using only this clinical assessment as a guiding line.

The contact surface of the cuff against the trachea, the residual volume and the elastic properties of the cuff are of great importance in clinical practice. These factors have been analysed by Carroll *et al.* (1969). Lomholt (1967) has constructed a new cuff with a large volume and has described a method for controlled cuff pressure. With this method the pressure exerted against the tracheal wall can be measured objectively. The same author has also shown, as did Adriani and Phillips (1957) that the trachea is just closed when the lateral pressure of the cuff is equal to the pressure inside the trachea. At the high insufflation pressures which are sometimes necessary in the treatment of exacerbations of chronic pulmonary diseases, this means that the lateral pressure from the cuff can need to be 60–70 cm H_2O, which involves a large risk of damage in these cases.

The problem of the pressure of the inflated cuff against the tracheal wall is similar in prolonged endotracheal intubation and tracheostomy. In this series a secondarily tracheostomized patient (case 180) who was treated with IPPV for 3 weeks developed such pronounced pressure necrosis in the trachea from the cuff of the tracheal cannula that it resulted in rupture of the trachea (Plate IV: 20 a, b.).

Artificial ventilation is considered by a number of authors (Allen and Steven, 1965, Fearon *et al.*, 1966, Harrison and Tonkin, 1968) to cause movements between the endotracheal tube and the larynx. This has also been pointed out by Way and Sooy (1965). Abbott (1968) reported, however, that laryngeal scarring was less common in patients who had undergone artificial ventilation. No direct comparisons could be made between patients who had undergone and those who had not undergone treatment with a respirator in this study, since only a few were not given artificial ventilation.

ad D. *A healing time* exceeding 1 month was noted in 33% of adult patients and 10% of infants and children in group F_2 in the follow-up series. This time exceeded 1 month, however, in 50% of patients with drug poisoning and miscellaneous indications for endotracheal intubation and in 23% of post-operatively treated adult patients.

The 2 former categories of indications were overrepresented in group F_2 in relation to the total follow-up series. A healing time of more than 1 month would therefore seem to be somewhat less common for the follow-up series as a whole.

Granuloma formation occurred in all patients in group F_2 for whom the healing time exceeded 1 month, with the exception of one patient (case 256), and in only 3 patients for whom it was less than 1 month.

In the children in group F_2 no postintubation granulomas were observed during the healing course.

Postintubation granulomas which there was reason to remove developed in 7 adult patients (2.6%) out of 267 in the follow-up series, while none of the 45 infants and children in the same series underwent removal of granulomas.

Hilding and Hilding (1962) have shown experimentally that regeneration of epithelium in superficial ulcerations takes place from the basement membrane when this is intact. When the basement membrane has been destroyed, on the other hand, a considerably slower healing process takes place from the edges of the ulcerated tissue.

This is in agreement with the observation in the present study that the healing process in deeper mucosal lesions (grades III–IV) more often took place via a stage of granuloma formation than in more superficial lesions (grades I–II). Epstein and Winston (1957) write: "... abrasion of the vocal process, 'Intubation Contact Ulcer', senile granuloma and the pedunculated granuloma are successive stages in the ultimate pathogenesis of intubation granuloma". The majority (93%) of the observed granulomas in this investigation regressed by a gradual decrease in size and did not become pedunculated before they finally disappeared, usually without sequelae. Epstein and Winston (1957) also state that the healing process can develop to a stage at which the base is so narrowed that auto-amputation follows. No cases of such spontaneous healing were observed in this study.

Healing with granuloma formation was more pronounced on the right side than on the left, and usually the granuloma disappeared later from this side (Plate II: 8 a–d; 9 a-e; 10 a–c; Plate III: 12 a–c; 13 a–c). A clear predominance of right-sided localizations of postintubation granulomas is also found in the presentation by Epstein and Winston (1957). The endotracheal tube is usually fixed at the right corner of the mouth and therefore lies to the right of the tongue inside the oral cavity. The tube is thereby easily forced to become reshaped in the frontal plane in the larynx to follow the airway, whereby a greater pressure is exerted against the right side of the larynx than against the left, which explains this circumstance. The endotracheal tube designed by the author for prolonged intubation is for this reason also curved laterally. This means that the tube lies in the midline of the larynx if the oral part is fixed at the right corner of the mouth and the tube lies to the right inside the oral cavity.

In view of the high frequency of spontaneous healing of postintubation granulomas, it is probable that also after endotracheal intubation anaesthesia healing takes place via a stage of granuloma formation more often than is usually observed.

From the above it is evident that conservative therapy can be used to advantage as long as the granuloma does not cause the patient considerable discomfort, since the chance of it disappearing spontaneously is large. What form the healing course would have taken if they had been removed surgically at an early stage cannot be stated since there is no comparative material. After extirpation of a granuloma which has become pedunculated there is only a negligible wound surface, which reduces the chance of recurrence.

The reason that a small number of primarily formed postintubation granulomas increased in size continuously is difficult to explain. Unfavourable healing conditions probably played a large role. Repeated trauma to the vocal process as a result of vocal misuse is accepted as a principal aetiological factor in this respect (Jackson, 1953). In one of the patients of this study (case 190) one of the granulomas was localized subglottically in the lateral posterior area, however (Plate IV: 17) and was not submitted to such trauma.

In one case (case 50) the granuloma was located on the anterior part of the vocal cord, clearly as a result of damage at this site after an emergency intubation. In the other patients with "irreversible granuloma" the intubation procedure was hardly traumatic.

Fibrous scar formation in the larynx occurred in 1 adult patient (case 287; Plate IV: 15 a–c) in group F_2 in the follow-up series. No further cases of this kind were observed in the remaining adult patients in that series, and the frequency of this complication was less than 0.5%. Similar but more pronounced cases have been reported previously both after prolonged endotracheal intubation (Minnigerode, 1968) and after intubation anaesthesia (Proctor and Edgerton, 1959). Bryce *et al.* (1968) have described, further, subglottic laryngeal stenosis in adult patients after prolonged endotracheal intubation.

In the present investigation it was the only serious laryngeal complication which occurred after prolonged endotracheal intubation of adult patients, and it could probably have been prevented if an anatomically correct tube had been available.

In 3 infants and children (cases C2, C3 and C20) in group F_2, fibrous scar formation occurred. No further complications of this kind occurred in the other infants and children in the follow-up series. The frequency of patients with fibrous laryngeal stenosis was 6.7%, in whom 4.4% were subglottic. This figure is in good agreement with the frequencies in other series (Table 3). These three complications, however, occurred in the first 20 infants and children treated with prolonged endotracheal intubation when little experience has been obtained of such treatment. None of the 25 infants and children who were treated last had any disabilities as a result of prolonged intubation, and the observation that the complication frequency decreased when the method had been more fully developed is in agreement with experience from other hospitals (Stocks, 1968) (Table 3).

The cause of acute damage giving rise to a healing course with scar formation has been discussed previously. The subglottic stenoses (cases C2 and C20) could probably have been avoided if tubes with a smaller external diameter had been used.

The glottic web (case C3) was the result of prolonged uncontrollable general convulsions. With the excessive laryngeal motor activity which occurred in this way it would probably have been better to perform a tracheostomy primarily in this case.

The result of the classification of acute damage correlated to healing time and late complications will be discussed in Chapter VIII (see p. 100).

Vocal disturbances for 1 week or more occurred in slightly less than half of the adult patients who underwent prolonged endotracheal intubation alone. In 16% the vocal disturbances persisted for more than 1 month. This figure is lower than the observed healing frequency with granuloma formation, which as a rule gave a healing time considerably exceeding 1 month. The reason for this was that in many patients with small reversible granulomas these often gave no noticeable vocal change. The reversible granulomas were, however, the principal causes of vocal disturbances.

In children the voice returned to normal, as a rule, more quickly than in adults, which was associated, among other things, with the fact that no granuloma formation occurred. Among the tracheostomized children there were two who had vocal disturbances for more than 1 month after decannulation. One infant (case C45) who underwent an operation for oesophagotracheal fistula was thus troubled with increased mucus formation in the airway and sounded "rattly", and the other was a child (case C3) in whom, as mentioned previously, healing took place with a glottic web which gave permanent moderate hoarseness.

Chapter VI

LATE DAMAGE IN THE LARYNX AND TRACHEA FOUND AT FOLLOW-UP EXAMINATION

This investigation was performed after a mean observation period of 13½ months (SD=8.5; range 3 months to 3 years and 6 months).

A. *Pathological findings in the larynx*

1. *Adults*

The status of the larynx at follow-up examination of 267 adult patients can be seen in Table 22. A normal status was observed in 246 patients and some form of pathological change in 21.

In 14 of these patients it was considered probable that prolonged endotracheal intubation had caused the laryngeal changes. These consisted in 3 cases (cases 21, 146 and 206) of internus paresis and in 2 cases (cases 26 and 322) of transversus paresis. Two of these patients (cases 21, 322) were already slightly hoarse before the period of intubation and noticed no change after this period. In 1 patient (case 190, Plate IV: 17) an asymptomatic subglottic granuloma was found, in 3 patients (cases 43, 172 and 248) fragments of degenerated postintubation granulomas and in 3 patients (cases 3, 23 and 92) small atrophic scars on the medial side of the vocal process. A suggestion of a stenosis 5 mm below the plane of the vocal cord persisted after the excision of scar tissue in 1 patient (case 287, Plate IV: 15 e) and an asymptomatic cyst on the vocal process was observed in 1 patient (case 256, Plate III: 14 b).

In 7 of the patients presented in Table 22 the pathological findings were not considered to have been caused by prolonged endotracheal intubation. Four of these patients had paresis of the recurrent laryngeal nerve after an intrathoracic operation, 1 patient had bilateral paresis of the recurrent laryngeal nerve before the period of intubation and 2 patients had acute laryngitis at the follow-up examination.

2. *Infants and children*

The status of the larynx can be seen in Table 23. A normal status was observed in 41 infants and children (91%) and some form of pathological changes in 4 of them (9%).

The condition of 3 of these patients (cases C2, C3 and C20) has been described in part previously (see p. 58).

The 2 children with subglottic stenoses (cases C2 and C20) had no respiratory difficulties at their follow-up examinations 2 years and 1 year and 5

TABLE 22.

Status of the larynx at follow-up examination in adult patients.

Status of the larynx	Thoracic surgery	General surgery	Drug poisoning	Miscell-aneous	No. of patients
Normal	187	11	26	22	246 (92%)
Pathological	16	–	3	2	21 (8%)
Considered to be connected with prolonged endotracheal intubation					
Internus paresis	3	–	–	–	3
Transversus paresis	1	–	1	–	2
Subglottic granuloma	1[1])	–	–	–	1
Remnant of degenerated postintubation granuloma, viz. mucosal tag on the vocal process	3	–	–	–	3
Small atrophic scar on the vocal process	3	–	–	–	3
Small remnant of fibrous subglottic web	–	–	1[2])	–	1
Cyst of the vocal process	–	–	1[3])	–	1
Considered to have no connection with prolonged endotracheal intubation					
Recurrent laryngeal nerve paralysis	4	–	–	1	5
Acute laryngitis	1	–	–	1	2

[1]) Case 190; Plate IV: 17.
[2]) Case 287; Plate IV: 15 e.
[3]) Case 256; Plate III: 14 b.

TABLE 23.

Status of the larynx at follow-up examination in infants and children.

Status of the larynx	Age		No. of patients
	< 1 year	≥ 1 year	
Normal	18	23	41 (91%)
Pathological	2	2	4 (9%)
Considered to be connected with prolonged endotracheal intubation			
Fibrous subglottic stenosis	1[1])	1[2])	2
Fibrous glottic web	–	1[3])	1
Considered to have no connection with prolonged endotracheal intubation			
Cystic hygroma involving the aryepiglottic fold	1	–	1

[1]) Case C2.
[2]) Case C20; Plate V: 25 d.
[3]) Case C3; Plate V: 26 b.

months, respectively, after the end of the intubation period, and had had no difficulty in expectoration or respiration during upper respiratory infections. Plate V: 25 d shows the laryngeal status 1 year and 5 months after the period of intubation in the child (case C20) who had the most pronounced subglottic stenosis. The laryngeal status in the boy (case C3) who had a permanent scar starting at the left vocal process and bridging the left part of the interarytenoid space can be seen in Plate V: 26 b, 2 years and 8 months after the period of intubation. The boy still had some stridor on physical effort such as during games and athletics, but no respiratory difficulties at rest or on moderate physical effort.

One child (case C28) had been treated with prolonged endotracheal intubation in connection with surgical removal of a large hygroma which infiltrated the pharyngeal wall and parts of the larynx. These laryngeal changes thus had no relationship with prolonged endotracheal intubation.

B. *Pathological findings in the trachea*

1. *Adults*

Radiographic examination of the trachea was performed on 250 adult patients of the total 267 followed up (Table 24). In 226 patients (90%) the tracheal radiogram appeared normal, and in 24 patients (10%) various patho-

Table 24.

Tracheal radiography at follow-up examination in adult patients.
No. of patients treated with prolonged endotracheal intubation only: 206.
No. of patients treated with prolonged endotracheal intubation plus tracheostomy: 44.

Tracheal radiography	Thoracic surgery	General surgery	Drug poisoning	Miscellaneous	No of patients
Normal	183	7	25	11	226 (90%)
Pathological	14	2	1	7	24 (10%)
Considered to be connected with prolonged endotracheal intubation					
Stenosis	1	–	–	–	1
Minor irregularities in the wall of the trachea	1	–	–	2	3
Considered to be connected with tracheostomy					
Stenosis	10	1	1	4	16
Minor irregularities in the wall of the trachea	2	–	–	1	3
Considered to have no connection with prolonged endotracheal intubation or tracheostomy					
Malformation of the trachea	–	1	–	–	1
Not examined	6	2	3	6	17

logical conditions were discovered. Among the 250 radiographically examined patients, 41 had been tracheostomized after initial prolonged endotracheal intubation, and 3 on previous occasions.

In the group of patients treated with prolonged endotracheal intubation alone (206 cases), only 1 tracheal stenosis was found (case 79), slightly below the level of the cricoid ring, and in 3 patients (cases 139, 177 and 208) minor irregularities in the tracheal wall were seen.

In the group of patients subjected to prolonged endotracheal intubation plus tracheostomy (44 cases), as many as 16 showed tracheal stenosis at different levels, and in 3 patients there were minor irregularities in the tracheal wall.

Plate IV: 17 and 18 a show 2 pronounced tracheal stenoses (cases 63 and 209) and Plate IV: 19 a less pronounced stenosis (case 232).

Finally, 1 patient (case 235) had a malformed trachea before the period of prolonged intubation and secondary tracheostomy.

In Table 26 the constriction of the tracheal lumen, calculated in per cent of the cross sectional area of the intact lumen, is given for the 17 stenoses which were observed in adult patients, and for 1 stenosis in an infant. The mean constriction of the lumen comprised 55% (range 31–92%).

2. *Infants and children*

Radiographic examination of the trachea was performed on 41 children of the total 45 followed up (Table 25). In 36 patients (88%) the tracheal radiogram appeared normal, and in 5 patients (12%) some form of pathological change was observed.

In the group of children treated with prolonged endotracheal intubation alone (30 cases), no pathological changes were observed which could be related to the endotracheal intubation.

In the group of children subjected to prolonged endotracheal intubation plus tracheostomy (11 cases), 2 tracheal stenoses were found (cases C28 and C55). Patient C28 had been tracheostomized after initial prolonged endotracheal intubation, and had worn a cannula for 1 year. In patient C55, the tracheal stenosis occurred after primary tracheostomy. This gave reason for prolonged endotracheal intubation followed by secondary tracheostomy. At the follow-up examination the patient still wore the cannula and has therefore not been included in Table 26.

In 3 patients (cases C42, C45 and C48) a "soft tracheal wall" was noted, which could neither be related to prolonged endotracheal intubation nor to tracheostomy, but was a residual condition following tracheo-oesophageal malformation in 2 patients (cases C45 and C48) and a vascular anomaly in 1 patient (case C41).

C. *Vocal disturbances*

1. *Adults*

The voice was considered to be normal in 250 (94%) of 265 adult patients in whom an assessment was possible. Only 2 patients (cases 180 and 278)

Table 25.

Tracheal radiography at follow-up examination in infants and children.
No. of patients treated with prolonged endotracheal intubation only: 30.
No. of patients treated with prolonged endotracheal intubation plus tracheostomy: 11.
No pathological changes were found in the trachea following prolonged endotracheal intubation only.

Tracheal radiography	Age		No. of patients
	≤ 1 year	≥ 1 year	
Normal	15	21	36 (88%)
Pathological	3	2	5 (12%)
Considered to be connected with tracheostomy			
Stenosis	1	1	2
Considered to have no connection with prolonged endotracheal intubation or tracheostomy			
Soft tracheal wall	2	1	3
Not examined	2	2	4

Table 26.

Tracheal stenoses found at the follow-up examination.

Case nos.	Smallest cross-sectional area of the stenotic lumen (mm^2)	Cross-sectional area of intact lumen (mm^2)	The stenosis in % of the cross-sectional area of the intact lumen
19	227	450	41
32	113	305	63
35	240	385	38
43	269	388	31
51	102	372	73
79[1])	132	245	46
115	19	208	91
129	120	254	53
146	107	318	66
178	92	170	46
189	143	232	38
190	38	170	77
209	20	247	92
232	125	240	48
262	198	330	40
277	173	298	42
322	99	194	49
C28	17	42	60

[1]) The only stenosis after prolonged endotracheal intubation alone among 236 patients. The remaining stenoses had developed among 44 adults and 11 children after prolonged endotracheal intubation plus tracheostomy.

could not be assessed; the reason being that both of them wore cannulae because of their basic disease at the follow-up examination (Table 27). In 10 patients (4%) the voice was assessed as slightly hoarse. In 3 of these patients (cases 21, 146 and 206), there was slight internus paresis, in 1 patient transversus paresis, in 2 patients (cases 128 and 275) slight laryngitis, in 2 patients (cases 19 and 232) tracheal stenosis and in 2 patients (cases 289 and 294) there was a residual slight vocal disturbance after the period of intubation without any visible pathological change (cases 289 and 294).

In 5 patients (2%) (cases 47, 127, 195, 200 and 316) the voice was assessed as hoarse, which was due in all cases to paresis of the recurrent laryngeal nerve. This was caused in 4 cases by intrathoracic operations, and in 1 case it was also present before the period of intubation. Thus in none of these 5 patients had prolonged endotracheal intubation caused the vocal disturbances.

2. *Infants and children*

The voice was found to be normal in 40 (96%) of 42 infants and children in whom assessment was possible. In 3 cases (cases C36, C44 and C55) assessment was not possible because the patient was still wearing a tracheal cannula at the follow-up examination. The reason for this in all cases was the patient's basic disease (Table 28).

In 1 patient (case C45) the voice was slightly hoarse. The same patient was assessed at radiographic examination to have a "soft tracheal wall" as a residual condition after surgical repair of an oesophagotracheal fistula.

Finally, 1 patient (case C3) was hoarse owing to the laryngeal scar mentioned previously (see p. 72), which developed after prolonged endotracheal intubation.

D. *Discussion*

ad A. Despite the fact that on examination within the first week after the period of intubation macroscopic *laryngeal changes* of different degrees of severity (see p. 52) were found without exception in all patients treated with prolonged

Table 27.

Voice at follow-up examination in adult patients.

Voice	Thoracic surgery	General surgery	Drug poisoning	Miscellaneous	No. of patients
Normal	192	10	28	20	250 (94%)
Slightly hoarse	7	1	–	2	10 (4%)
Hoarse	4	–	–	1	5 (2%)
Tracheostomy cannula *in situ*	–	–	1	1	2
No. of patients	203	11	29	24	267

Table 28.

Voice at follow-up examination in infants and children.

Voice	Age		No. of patients
	< 1 year	≥ 1 year	
Normal	17	23	40 (96%)
Slightly hoarse	1	–	1 (2%)
Hoarse	–	1[1])	1 (2%)
Tracheostomy cannula *in situ*	2	1	3
No. of patients	20	25	45

[1]) Case C 3; Plate V: 26 b.

endotracheal intubation, and despite the fact that the healing time often exceeded 1 month (Fig. 10), very few residual lesions of importance were found at the follow-up examination (Tables 22 and 23).

Of the 5 adult patients who had slight laryngeal pareses in 3 of them and possibly the other 2, these probably occurred in connection with prolonged endotracheal intubation.

In 2 patients (cases 190 and 256), residual lesions (subglottic granuloma and cyst on the vocal process, respectively) in the larynx were found at the follow-up examination. These were removed surgically and healed without complications.

In the 3 patients who still had remnants of degenerated postintubation granulomas on the vocal process, these were healed at a further examination a few months after the follow-up examination.

The 3 patients who had minor scars on the vocal process had no symptoms. The scars were so small that they would probably have been overlooked if special attention had not been directed towards this area at the examination.

In the woman (case 287) who had developed a fibrotic scar in the posterior part of the larynx during the healing course after a lesion of grade IV, and in whom the scar tissue had been extirpated 4 months before the follow-up examination, only a very small mucosa-covered ridge remained (Plate IV: 15 e). Her voice had become normal and she had been able to resume her engagements as an actress.

Among the 3 children who had developed fibrotic scars in the larynx as a result of damage following prolonged intubation, 2 of them, after long periods of convalescence, had no symptoms from the residual lesions which were observed. The third child (case C3) had some stridor on physical effort.

Thus it can be said that no serious permanent laryngeal changes occurred in the adult patients, that 2 children still had asymptomatic subglottic scars

1½ and 2 years after the period of intubation, and that 1 child still had a glottic web which gave mild symptoms more than $2\frac{1}{2}$ years after the treatment with an endotracheal tube.

ad B. *Tracheal changes* occurred in 10% of the adult patients and in 12% of the children. Stenosis was the most common change, and in a small number of cases irregularities were observed in the tracheal wall.

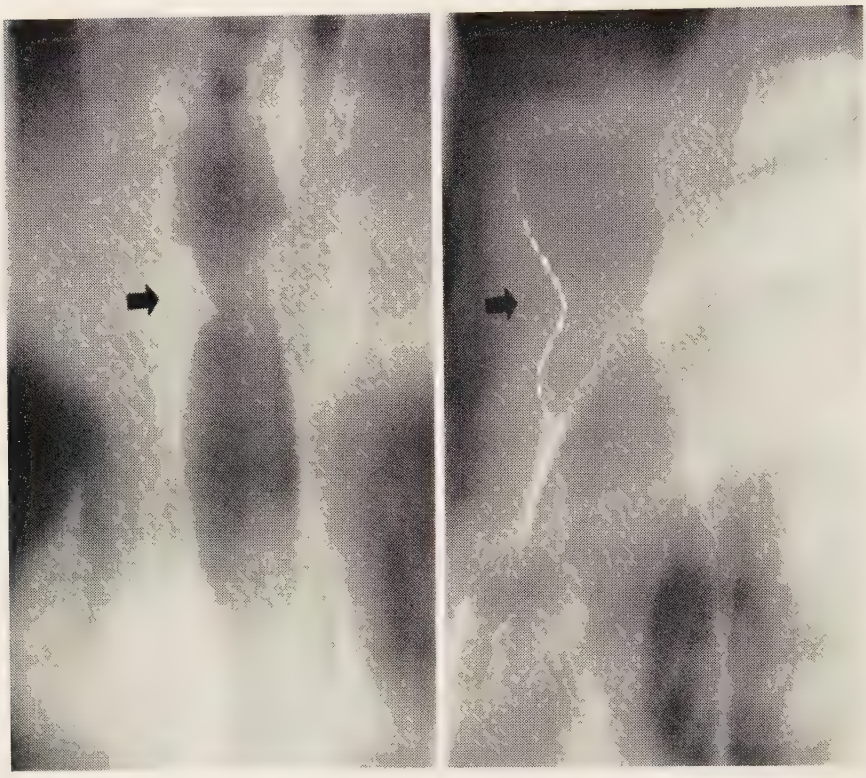
Among the 206 patients who were subjected to prolonged endotracheal intubation alone, only 1 was found with tracheal stenosis (0.5%), and 3 with irregularities of the tracheal wall. These findings probably constituted residual conditions following prolonged endotracheal intubation and it is probable that they were caused by the inflated cuff of the endotracheal tube.

Among the 44 adult patients who were subjected to prolonged endotracheal intubation plus secondary tracheostomy, or had been tracheostomized on a previous occasion (41 and 3 patients, respectively), no fewer than 16 patients had tracheal stenoses (36%) and 3 had irregularities in the tracheal wall. The duration of the tracheostomy in 8 of the patients who developed stenosis was $\leq$ 5 days. It is probable that the tracheostomy had caused the great majority of the stenoses. It is also conceivable that tracheostomy preceded by a period of prolonged endotracheal intubation might mean an increased risk of stenosis compared with primary tracheostomy. This would seem fairly unlikely, however, since the frequency of stenosis in this group is in very good agreement with results published recently by other authors who have analysed series of tracheostomized patients. Kucher *et al.* (1967) and Stoeckel (1968) thus report a constriction of the lumen by ⅓ or more in 56% and 32%, respectively, in their studies of late results of tracheostomy.

Two patients in the present series had a stenosis of about 90%, with severe symptoms of obstruction. Both stenoses had to be corrected surgically. One woman (case 190) had a stenosis of 77% (Plate IV: 17). This patient had a partial hemiparesis and moved very little, so that in spite of the severe stenosis her ventilation was, in general, adequate for her needs. She had stridor on physical effort, and during upper respiratory infections she had great difficulty in expectoration. One man (case 51, Fig. 14) with a stenosis of 73% had no major symptoms from this. Among the remaining patients with tracheal stenosis, many reported difficulty in expectoration during upper respiratory infections, but otherwise they had no or surprisingly little discomfort. This observation is in good agreement with the experience that a tracheal stenosis does not usually produce symptoms until it comprises 50–75% of the original lumen (Kucher *et al.*, 1967, Flemming and Hommerich, 1968, Stoeckel, 1968). Stoeckel (1968) also reports that less severe stenoses have given rise to symptoms in a few patients.

In infants and children subjected to prolonged endotracheal intubation alone, no tracheal changes were observed.

In 1 infant, the prolonged endotracheal intubation had been followed by



a b

FIG. 14.—Case 51: 43-year old man with aortic valvular disease subjected to implantation of a Starr ball valve. He was intubated with a 13.0 mm (e.d.) BOC reinforced latex tube for 33 hours, after which he was tracheostomized and wore a tracheal cannula for 3 days.
a. Frontal projection tomogram showing stenosis (arrow) at the level of the tracheostomy 3 years after the acute stage.
b. Lateral projection tomogram showing the same stenosis (arrow).

tracheostomy and the patient wore a cannula for 1 year, after which it was removed. This infant had a cystic hygroma of the neck. A stenosis below the level of the tracheostoma was found at the follow-up examination but the patient had no definite symptoms of obstruction.

One child underwent therapeutic prolonged endotracheal intubation because of a soft stenosis in the trachea which developed after primary tracheostomy. Retracheostomy was necessary later, and the child wore a cannula at the follow-up examination.

Severe fibrous tracheal stenoses can occur, but mild and moderate stenoses of this kind are more common after tracheostomy. This has only been observed during recent years. One reason for this is the increase in tracheostomies in the last 10 years with a concomitant increase in late complications. Another

Location	Adults Stenosis considered to be connected with:		Infants and children Stenosis considered to be connected with:	
	Prolonged endotracheal intubation out of 206 patients	Tracheostomy out of 44 patients	Prolonged endotracheal intubation out of 30 patients	Tracheostomy out of 11 patients
Glottic			1	
Subglottic	1	–	2	–
Tracheostomy level (and immediately over and below)	1	13	–	–
Below tracheostomy level (Level of the cuff or the tip of the cannula)	–	3	–	2
Total	2	16	3	2

FIG. 15.—Stenoses in the larynx and trachea found at follow-up examination of 236 patients subjected to prolonged endotracheal intubation alone and 55 patients subjected to prolonged endotracheal intubation plus tracheostomy.

reason is obviously that the symptoms usually only become manifest in pronounced cases. It has also happened that the respiratory symptoms have been misinterpreted as bronchial asthma (STOECKEL, 1968) and it is especially easy to overlook a stenosis in a patient who has undergone primary tracheostomy and has been treated with a respirator for a respiratory disease (MOLLARET *et al.*, 1962, FAIRLEY, 1968). In patients with chronic pulmonary insufficiency a less pronounced stenosis can also be expected to be of clinical importance long before it would have been in a person with healthy lungs.

ad A and B. Fig. 15 shows the localization of the fibrous stenoses which were discovered in the larynx and trachea in the follow-up series.

Most striking is the high frequency of stenosis at the level of the tracheostoma in tracheostomized adult patients. At this level the stenosis was moderate, and usually the lumen had assumed a triangular shape with one of the corners directed ventrally (Plate IV: 19). Tracheostomy always gives rise to a defect in the cartilaginous skeleton. The presence of a cannula in the stoma for some time creates a prerequisite for the formation of a stenosis during the healing course (NELSON, 1958, PEARSON, 1968).

In the adult patients fibrous tracheal stenoses caused by the cuff were fewer, but on the other hand the most pronounced. Two of these stenoses are shown on Plate IV: 17 and 18 a.

In striking contrast to the high frequency of stenosis probably caused by tracheostomy, is the low frequency of stenosis in the larynx and trachea after prolonged endotracheal intubation alone in adult patients.

In children the situation was rather different. One infant and 1 child developed tracheal stenoses which were obviously caused by tracheostomy, while 1 infant and 2 children among the 20 who first underwent prolonged endotracheal intubation had stenotic scars in the larynx. In the 25 infants and children who were last treated with prolonged endotracheal intubation, no stenoses developed. The tendency towards a reduction of these complications with further improvements in the management of these patients is also evident in the study of Stocks (1968). Tracheostomy in infants and children gives rise to many problems (see literature review), but fibrous tracheal stenosis is considered by some authors to be less frequent in children than in adults (Oppliger, 1968). It is worthy of mention, however, that tracheal stenosis with a fatal outcome following tracheostomy was observed in 2 children within the region covered by the University Hospital, Uppsala, during 1967–1968.

ad C. *Vocal disturbances* were present in a relatively high frequency (16%) 1 month after the period of intubation in adult patients subjected to prolonged endotracheal intubation alone (see p. 59).

At the follow-up examination, however, only 15 adult patients (6%) had vocal disturbances. In 9 of these patients the disturbances could not be related to the prolonged intubation. In 6 patients the intubation may have caused mild vocal disturbances in the form of phonasthenia or slight hoarseness. So-called "myopathic pareses" (internus paresis and transversus paresis) in the larynx were found in 4 of these, 2 of whom, however (cases 21 and 322), reported that their vocal disturbances had been present before the period of intubation. If these last 2 patients are excluded, there remain 4 patients out of 265 (1.5%) in whom mild vocal disturbances were probably caused by prolonged endotracheal intubation. None of these patients, however, had such symptoms as to cause them to seek medical advice of their own accord.

Among the infants and children, vocal disturbances were found at the follow-up examination in only 1 infant and 1 child (4%). The infant (case C45) had a "soft tracheal wall", which had no relationship with prolonged endotracheal intubation. The child (case C3) had moderate hoarseness due to the scar formation in the larynx described previously (see p. 72). Permanent vocal disturbances due to prolonged endotracheal intubation thus comprised about 2% in this group.

These results are based on the patient's own assessment and the author's opinion of the voice. Only in exceptional cases was stroboscopy performed.

This study would seem to provide a good picture for clinical evaluation of vocal disturbances after prolonged endotracheal intubation.

Subclinical vocal disturbances, which can only be recorded by more objective methods, may possibly have been present in several cases.

Chapter VII

POST MORTEM STUDIES OF DAMAGE FOLLOWING PROLONGED ENDOTRACHEAL INTUBATION AND IN A NUMBER OF CASES SECONDARY TRACHEOSTOMY

By

Roland Bergström[1]) and Carl-Eric Lindholm

Macroscopic and microscopic examinations were performed on 78 specimens, and on 1 further specimen microscopic examination alone.

In preparation of the laryngeal specimens for post mortem examination, some of them were damaged, but none of them had to be excluded for this reason. In 16 specimens less than $^2/_3$ of the length of the trachea was available for examination. At the histological examination a few sections in some specimens could not be evaluated with certainty and were excluded.

A. *Macroscopic evaluation of damage in the larynx and trachea*

1. *Patients subjected to prolonged endotracheal intubation alone*

a. Adults

Macroscopically observed ulceration and necrosis were localized mainly to four regions (Fig. 16). No patient had damage which comprised a continuous area of more than $^1/_3$ of the larynx in cross-section. In the trachea, on the other hand, 2 circumferential mucosal lesions were observed, one of which is shown in Fig. 17 b.

Table 29 gives the incidence of macroscopic ulceration or necrosis in the different regions of the larynx and trachea in this part of the post mortem series. Only 3 out of 33 patients had superficial ulcers in the interarytenoid area. In 26 out of 33 patients ulceration or necrosis of varying depth was seen on the medial sides of the arytenoid cartilages, and in 33 out of 34 such lesions were observed within the inner postero-lateral part of the cricoid cartilage. Eight patients out of 26 showed corresponding lesions localized mainly to the

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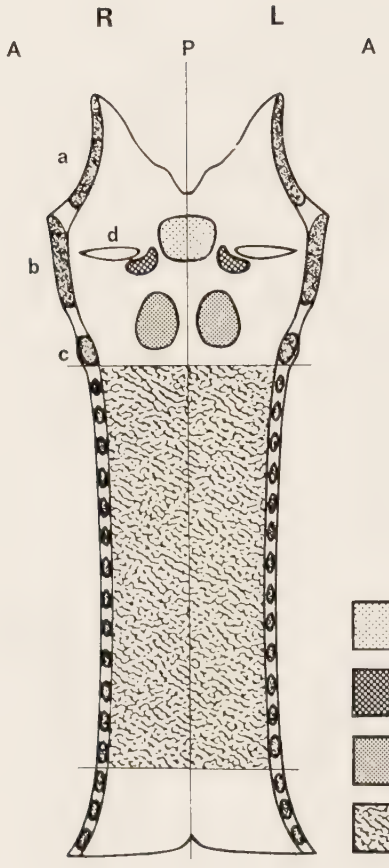

FIG. 16.—Schematic drawing showing the laryngotracheal specimen, split along the anterior midline
A: anterior midline. P: posterior midline. R: right L: left.
a: epiglottis. b: thyroid cartilage.
c: cricoid cartilage. d: sinus of Morgagni.

Location of macroscopic ulceration or necrosis in the laryngotracheal specimen following prolonged endotracheal intubation, which was followed by tracheostomy in approximately half of the cases.
1. Interarytenoid area.
2. Medial side of the arytenoid cartilage.
3. Inner postero-lateral area of the cricoid cartilage.
4. Different levels in the trachea (mostly cuff level).

middle parts of the trachea. One membranous haemorrhagic laryngotracheitis was observed, in addition, in 1 patient in this group.

b. Infants and children

Ulceration was observed macroscopically in only 1 infant (case C53) in this part of the series (Table 29), and no appreciable necrosis in any of the infants or children. The localization of the laryngeal damage in this infant was the same as in the adult patients. The lesions were deep but comprised a continuous area of less than $\frac{1}{3}$ of the larynx in cross-section. Among the remaining infants and children subjected to prolonged endotracheal intubation alone, minor mucosal haemorrhages were observed in the larynx in most of them, but otherwise the mucosa was macroscopically intact.

No ulceration was seen in the trachea, and there were no signs of membranous laryngotracheitis.

a b

FIG. 17.—Case 149: 57-year old woman with bronchial asthma and cardiac insufficiency, intubated with a 12.4 mm (e.d.) PVC tube for 76 hours. She died with the tube *in situ*. The photograph shows the laryngotracheal specimen cut along the anterior midline.

a. Extensive necrosis of the mucosa covering the inner postero-lateral part of the cricoid cartilage (lower arrow) and minor mucosal lesions on the medial side of the vocal process (upper arrow).

b. Circumferential extensive mucosal lesions in the trachea probably caused by the inflated cuff.

TABLE 29.

Macroscopic ulceration or necrosis in different regions of the laryngotracheal specimen at post mortem examination of patients subjected to *prolonged endotracheal intubation alone.*

Location according to Fig. 16	Adults		Infants and children	
	No. of specimens studied	No. with macroscopic ulceration or necrosis	No. of specimens studied	No. with macroscopic ulceration or necrosis
Interarytenoid area (1)	33	3	9	0
Medial side of arytenoid cartilage (2)	33	26	9	1
Inner postero-lateral area of cricoid cartilage (3)	34	23	10	1
Different levels in trachea (usually cuff level) (4)	26	8	9	0

2. *Patients subjected to prolonged endotracheal intubation plus secondary tracheostomy*

a. Adults

Ulceration and necrosis was observed at similar locations in the larynx and in essentially the same frequency as in the patients treated by prolonged endotracheal intubation alone (Table 30). Thus such lesions were found in the interarytenoid area in 3 out of 31 patients, on the medial side of the arytenoid cartilage in 21 out of 31 and within the inner postero-lateral part of the cricoid cartilage in 21 out of 31 patients. In the trachea, as many as 24 out of 25 patients showed, in addition to the tracheostomy wound, ulceration or necrosis at the level of the inflated cuff of the tracheal cannula and/or laterally on the tracheal wall at the level of or slightly below the tracheostoma (Fig. 18). The ulceration at the cuff level often comprised that part of the circumference corresponding to the tracheal cartilage. Membranous laryngotracheitis was observed in 4 cases.

b. Infants and children

In 1 of the 2 children treated with prolonged endotracheal intubation and tracheostomized secondarily, dilatation of the trachea with posterior bulging of the pars membranacea was observed, and also ulceration with partial exposure of the cartilage in the remaining circumference of the trachea at the level of the cannula (Table 30, Fig. 19). No signs of membranous laryngotracheitis were seen.

TABLE 30.

Macroscopic ulceration or necrosis in addition to the tracheostomy wound in different regions of the laryngotracheal specimen at post mortem examination of patients subjected to *prolonged endotracheal intubation plus tracheostomy.*

Location according to Fig. 16	Adults		Infants and children	
	No. of specimens studied	No. with macroscopic ulceration or necrosis	No. of specimens studied	No. with macroscopic ulceration or necrosis
Interarytenoid area (1)	32	4	2	0
Medial side of arytenoid cartilage (2)	32	22	2	0
Inner postero-lateral area of cricoid cartilage (3)	32	23	2	0
Different levels in trachea (usually cuff level) (4)	26	25	2	1

FIG. 18.—Case C 36: 4-month old boy with congenital heart disease and pneumonia, intubated for $8^1/_2$ days (cf. Plate V: 24). Secondary tracheostomy was performed and he was given artificial ventilation via an uncuffed tracheal cannula for a further 3 months before he died. The photograph shows the laryngotracheal specimen cut ventrally. Laryngeal status normal. In the trachea a dilatation of the pars membranacea bulging posteriorly (left arrow) and mucosal ulceration with partly exposed cartilage at the same level (right arrow) are seen.

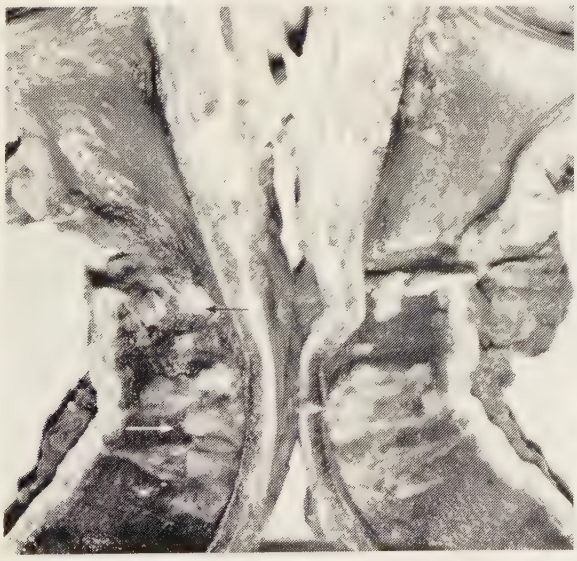

FIG. 19.—57-year old man with cardiac infarction and cardiac aneurysm who underwent resection of left ventricular aneurysm. Intubated during operation and then tracheostomized primarily. Treated with artificial ventilation for 5 days via the cuffed tracheal cannula before he died. The photograph shows the laryngotracheal specimen with extensive necrosis of the tracheal mucosa, especially at the level of the cuff, where the cartilage is exposed and partly eroded (lower arrow). On the lateral part of the tracheal wall at the stoma level the mucosa is also damaged (upper arrow).

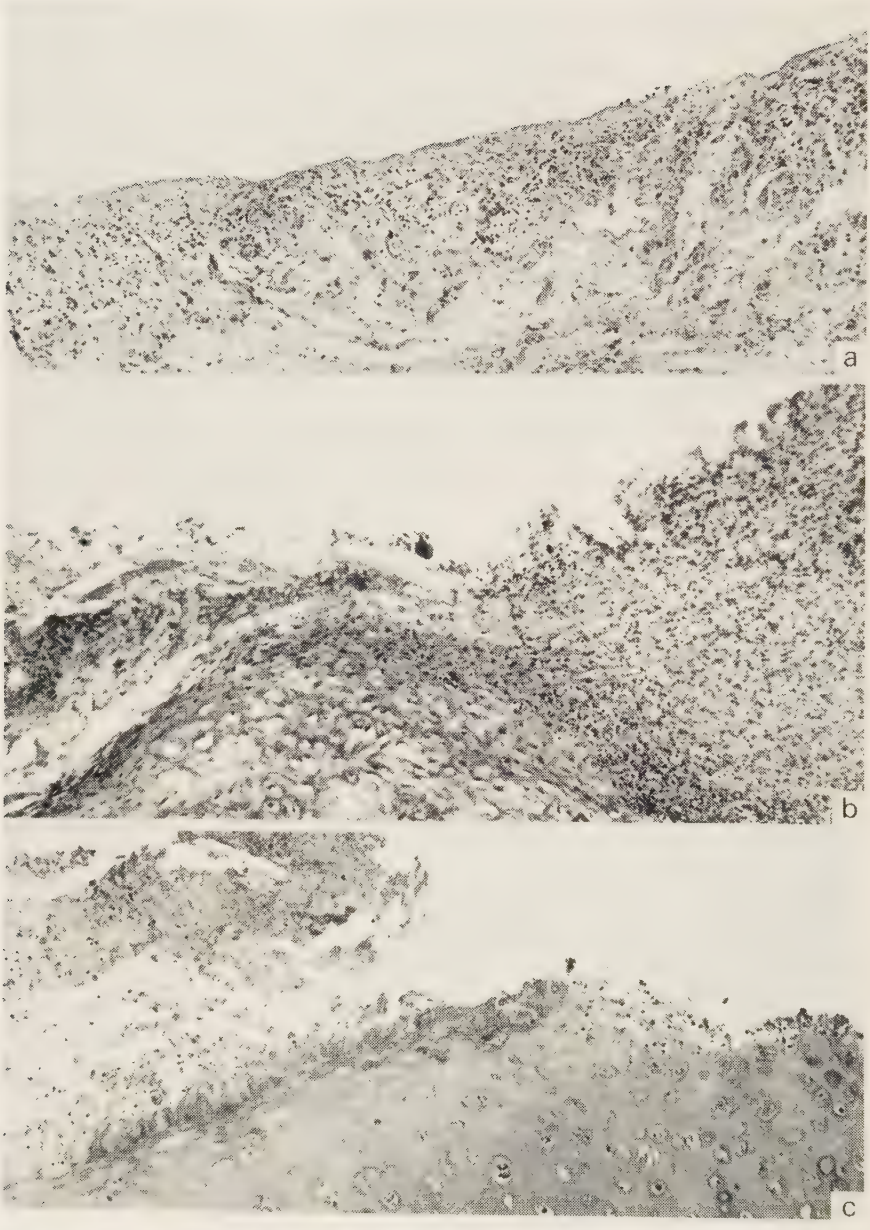

Fig. 20.—Sections 6 and 2 (cf. Fig. 9) showing different ulcers on the medial side of the arytenoid cartilage.

a. Ulceration (erosion) with retained basement membrane (van Gieson, approx. × 100).

b. Ulceration comprising the lamina propria but which has not penetrated the perichondrium (Hematoxylin-eosin, approx. × 100).

c. Ulceration which has penetrated the perichondrium (Hematoxylin-eosin, approx. × 100).

B. *Microscopic evaluation of damage in the larynx and trachea*

In all specimens examined, some form of mucosal change was observed. Fig. 20 shows postintubation damage with ulceration of 3 different depths (see p. 46) on the medial side of the arytenoid cartilage. Ulceration which had damaged the perichondrium and sometimes the cartilage was found in 31 specimens at one or more levels (Fig. 9). Necrosis and inflammation of the same depth occurred in 16 and 51 specimens, respectively.

1. *Patients subjected to prolonged endotracheal intubation alone*

a. Adults

The depth of the inflammation, necrosis and ulceration (see pp. 45 and 46) at the different levels (Fig. 9) can be seen in Table 31.

All of these types of changes were most pronounced in sections 2 + 6, corresponding to the medial side of the vocal process, and least pronounced in sections 1 + 5, corresponding to the interarytenoid region. In sections 3 + 7 and 4 + 8, corresponding to the cricoid level and the "cuff level" in the trachea, respectively, the changes were essentially of equal magnitude.

TABLE 31.

Microscopic examination of sections at different levels (Fig. 9) of the larynx and trachea in patients subjected to *prolonged endotracheal intubation alone*. Inflammation, necrosis and ulceration have been classified according to the scheme described on pages 45 and 46. The figure 1 refers to normal conditions and 2–4 increasing depth of the lesions.

Location of damage according to Fig. 9	No. of specimens[1]) studied	Depth of inflammation				Depth of necrosis				Depth of ulceration			
		1	2	3	4	1	2	3	4	1	2	3	4
Adults													
Sections 1 + 5	35	0	19	11	5	28	2	4	1	5	19	9	2
Sections 2 + 6	35	1	3	9	22	5	7	19	4	0	3	19	13
Sections 3 + 7	35	1	10	23	1	11	13	11	0	2	10	22	1
Sections 4 + 8	35	0	9	25	1	24	6	5	0	1	14	17	3
Infants and children													
Sections 1 + 5	10	1	5	2	2	8	2	0	0	1	7	0	2
Sections 2 + 6	9	0	3	4	2	1	5	3	0	0	4	4	1
Sections 3 + 7	10	0	3	6	1	6	2	2	0	0	7	3	0
Sections 4 + 8	8	0	4	4	0	5	3	0	0	0	5	3	0

[1]) Some sections at different levels had to be excluded because they were absent from the specimen or could not be evaluated with certainty.

b. Infants and children

The microscopic changes in the larynx and trachea did not differ essentially from those observed in the adult specimens (Table 31). Necrosis and ulceration comprising the perichondrium or cartilage was found with certainty in only 1 specimen. In another specimen, similar damage was found at the level 1 + 5, but this was probably an artifact.

2. *Patients subjected to prolonged endotracheal intubation plus secondary tracheostomy*

a. Adults

The occurrence of inflammation, necrosis and ulceration showed an essentially similar distribution in the larynx as in the patients treated with prolonged intubation alone. In the trachea, on the other hand, deep lesions were observed considerably more often than in the group treated only with prolonged endotracheal intubation (Table 32).

Table 32.

Microscopic examination of sections at different levels (Fig. 9) of the larynx and trachea in patients subjected to *prolonged endotracheal intubation plus secondary tracheostomy*. Inflammation, necrosis and ulceration have been classified according to the scheme described on pages 45 and 46. The figure 1 refers to normal conditions and 2–4 increasing depth of the lesions.

Location of damage according to Fig. 9	No. of specimens[1]) studied	Depth of inflammation				Depth of necrosis				Depth of ulceration			
		1	2	3	4	1	2	3	4	1	2	3	4
Adults													
Sections 1 + 5	29	2	9	10	8	24	2	2	1	9	9	9	2
Sections 2 + 6	30	0	4	3	23	13	3	8	6	2	2	17	9
Sections 3 + 7	30	1	1	24	4	12	6	12	0	1	5	23	1
Sections 4 + 8	30	0	1	15	14	3	8	12	7	1	1	20	8
Infants and children													
Sections 1 + 5	2	2	0	0	0	2	0	0	0	2	0	0	0
Sections 2 + 6	2	1	0	1	0	2	0	0	0	2	0	0	0
Sections 3 + 7	2	1	1	0	0	2	0	0	0	2	0	0	0
Sections 4 + 8	2	0	2	0	0	2	0	0	0	1	1	0	0

[1]) Some sections at different levels had to be excluded because they were absent from the specimen or could not be evaluated with certainty.

b. Infants and children

Specimens from only 2 children were included in this group, and neither of them showed deep necrosis or ulceration. In 1 case, however, inflammation which penetrated relatively deeply was observed.

C. *Discussion*

The causative mechanism for postintubation damage in the larynx and trachea and the localization of such damage, have been discussed previously (Chapter V: E.; p. 61). The post mortem examination verified the clinical findings (Figs. 16 and 17). The localization of the lesions was very constant and agreed essentially with the results of other studies (Bergström *et al.*, 1962, Hedden *et al.*, 1968).

The extent of the *macroscopically observed damage* on the medial side of the vocal process varied relatively little. Greater variation was noted in the extent of such damage along the circumference in the subglottic area. The least extensive lesions were localized bilaterally near to the posterior midline, and in many cases it was evident that the external diameter of the endotracheal tube had been small in relation to the lumen of the larynx. When endotracheal tubes with greater external diameters in relation to the lumen of the larynx were used, the lesions were more extensive and comprised a greater part of the lateral walls in the subglottic area (Fig. 17 a). If the external tube diameter had reached a boundary value equal to the greatest diameter in the lumen, a circumferential lesion would probably have occurred.

In the interarytenoid area there were very few necroses or ulcers which were visible to the naked eye. On the medial sides of the arytenoid cartilages and the inner postero-lateral areas of the cricoid cartilage, ¾ of the adults had pronounced necrosis or ulceration. In infants and children, on the other hand, only submucosal haemorrhages and a roughness of the mucosa were observed, except in 1 infant (case C 53), where deep ulceration was noted. The diagnosis in this case was diabetes mellitus and foetal hydrops. The mucosal resistance was greatly reduced in this patient. No great difference was found between the group treated with prolonged endotracheal intubation alone and that in which secondary tracheostomy was also performed. One difference was found between these groups, however, as regards tracheal lesions at the "cuff level". At this location practically all patients who also underwent secondary tracheostomy showed necrosis or ulceration, while these were noted in only ¼ of those subjected only to prolonged endotracheal intubation. In addition to the damage which was found below the tracheostoma in the secondarily tracheostomized patients, ulceration and slough were often observed in the lateral part of the tracheal wall at the level of the stoma or slightly lower (Fig. 18).

The aim of the *microscopic examination* was to determine the depth of the lesions. Practically all patients had inflammatory changes in all sections. Necrosis of varying depths also occurred in the majority, at least at one of the levels examined. Ulceration with penetration of the basement membrane of the mucosa was noted in practically all specimens.

In accordance with the macroscopic observations, the most penetrating changes were observed on the medial side of the arytenoid cartilages. The

right-sided lesions in this region were more pronounced than those on the left side, which agrees with the finding that right-sided granulomas were more frequent than left-sided. Local perichondritis in the region of necrotic or ulcerated tissue was noted in $^2/_3$ of all specimens at this level, but these included only 2 out of 11 infants and children. Ulceration which had penetrated the basement membrane of the mucosa was found at the same level in 63 out of 76 specimens, but these included only half of the specimens from infants and children. Ulceration which had penetrated the perichondrium on the medial side of the arytenoid cartilages was found in $^1/_3$ of the specimens; these included only 1 out of 11 specimens from infants and children.

In the subglottic area, local perichondritis was observed in 6 out of 77 specimens, and 1 of these was from an infant. Ulceration which had penetrated the basement membrane of the mucosa occurred in $^2/_3$ of the specimens at this level, but only in 2 cases had the ulceration penetrated the underlying perichondrium. No infants or children had ulceration reaching the perichondrium. The submucosal tissue in the subglottic area is relatively thick, whereas over the medial side of the arytenoid cartilages it is partly absent. This circumstance, combined with the fact that the contact surface of the tube was greater in the former than in the latter region, probably contributed to the finding that so few ulcers penetrated to the underlying cartilage at the level of the cricoid cartilage.

In the trachea, local perichondritis was found in 15 out of 75 specimens, but in none of the infants and children did this occur. Ulceration which had penetrated the basement membrane of the mucosa was observed in 51 out of 75 specimens, and these included 3 specimens out of 10 from infants and children. Ulceration with penetration of the perichondrium occurred in 11 out of 75 specimens, none of them from infants or children.

No definite difference was found with regard to laryngeal damage between the group of patients subjected to prolonged endotracheal intubation alone and those treated also with secondary tracheostomy. The tracheal lesions, on the other hand, clearly predominated in the latter group (ulceration with penetration of the basement membrane in approximately half of the patients treated with prolonged endotracheal intubation alone, and in 28 out of 32 patients subjected also to secondary tracheostomy).

The frequency of macroscopically observed ulceration and necrosis was somewhat lower than the frequency of those observed microscopically.

On comparing the frequency of ulceration which penetrated the perichondrium on the medial sides of the arytenoid cartilages in the post mortem series and the frequency of lesions which healed with granuloma formation in the follow-up series, these were found to be in good agreement. This does not necessarily mean that there is a correlation, but it would seem reasonable to assume that the two findings are related, especially as there was agreement with regard to side. Granulomas were seldom observed in the subglottic area, and damage to the perichondrium at this level was similarly rare.

The question of whether changes observed in a post mortem series are also representative of the surviving patient often arises. In an attempt to answer this question in the present study a comparison was made between patients who died with an endotracheal tube *in situ*, and those who had undergone prolonged endotracheal intubation but had been secondarily tracheostomized for some time (mean 10 days) before death and died with the cannula *in situ*. It is true that in both groups both the circulation and metabolism were often pathologically changed during the period of intubation, but if the agonal stage had been of great importance for the occurrence of damage, the deepest lesions would have occurred in those who died with the tube *in situ*. In addition, it can be assumed that the laryngeal lesions had healed in a few patients who wore a tracheal cannula for a long period after prolonged endotracheal intubation. This assumption is also supported by the results of statistical analysis of the material and should mean less pronounced damage in this category. The difference in depth of the laryngeal lesions between the two groups was negligible, however, which indicates that the agonal stage was of no decisive importance for the depth of the lesions.

Chapter VIII

SOME RELEVANT DATA BEFORE AND DURING THE PERIOD OF ENDOTRACHEAL INTUBATION CORRELATED TO THE POSTINTUBATION COURSE AND TO POST MORTEM FINDINGS

A. *Statistical analysis*

Adult patients in the follow-up series and the post mortem series were chosen for this analysis. Infants and children constitute a more heterogeneous material which deviates from the adults with regard to essential factors. It

TABLE 33.

Variables (regressors, i.e. independent variables, which were of possible importance for the postintubation course) and dependent variables (regressands) which characterized the postintubation course, and aslo post mortem findings in the larynx and trachea, together with their symbols, units and quantifications for the data processing.

Symbol of variable	Variable	Units and quantifications (Substituted values for not recorded data)
	Regressors	
X-1	Sex	male 1; female 2
X-2	Age	number of years of life
X-3	Thoracic surgery	
X-4	General surgery	
X-5	Drug poisoning	
X-6	Miscellaneous	
X-7	Duration of intubation	hour
X-8	Maximal external tube diameter	mm. (Not recorded 12.0)
X-9	Reinforced latex (BOC)	
X-10	Reinforced latex (Flotex)	
X-11	PVC (Portex)	
X-12	Magill red rubber	
X-13	Intubation difficulties	1 if, if not 0
X-14	More than one tube	1 if, if not 0
X-15	Dose of tubocurarine during operation	mg
X-16	Dose of tubocurarine postop.	mg
X-17	Dose of phenoperidine during operation	mg

TABLE 33 (*continued*)

Symbol of variable	Variable	Units and quantifications (Substituted values for not recorded data)
X-18	Dose of phenoperidine postop.	mg
X-19	Dose of haloperidol during operation	mg
X-20	Dose of haloperidol postop.	mg
X-21	Duration of artificial ventilation	hour
X-22	Pathogenic bacteria in airway	1 if, if not 0 (Not recorded 0.6)
X-23	Free respiration after extubation	
X-24	Respiratory obstruction after extubation necessitating tracheostomy	
X-25	Tracheostomy for expected prolonged artificial ventilation	
X-26	Duration of tracheostomy	day
X-27	Tracheostomy on an earlier occasion	1 if, if not recorded 0
	Regressands in the follow-up series	
X-28	Grade of acute postintubation damage	I–IV (cf. Chapter V:B); not recorded 0
X-29	Duration of healing time of acute postintubation damage in the larynx	day. Residual changes placed at 300 days
X-30	Vocal disturbances > 1 week after extubation	1 if, if not 0. (Not recorded 0.5)
X-31	Duration of vocal disturbances	week. Residual vocal changes at follow-up 99
X-32	Pathological changes in the larynx necessitating surgical treatment	granuloma 1; no changes 0; scar tissue 1; cyst 1
X-33	Subjective upper respiratory symptoms at follow-up	0 if, if not 1. (Not recorded 0.13)
X-34	Vocal disturbances at follow-up	normal 0; slightly hoarse 1; hoarse 2. (Not recorded 0.05)
X-35	Pathological changes in the larynx at follow-up	normal 0; pathological 1. (Not recorded 0.05)
X-36	Tracheal stenosis at follow-up	stenosis 1; no stenosis 0
	Regressands in the post mortem series	
X-37–X-44	Inflammation, sections 1–8	see Chapter III:B, 6
X-45–X-52	Necrosis, sections 1–8	see Chapter III:B, 6
X-53–X-60	Ulceration, sections 1–8	see Chapter III:B, 6
	Other variables	
X-61	Observation time	month
X-62	Period from extubation to death	day

was therefore considered unsuitable to include them in the same analysis. They would have been analysed separately if they had been more numerous.

Table 33 shows which variables were analysed, and gives their symbols, units and quantifications. Where data for a given regressor were not available, the approximate mean values (cf. last column in Table 33) were used instead for the data processing. With regard to variable X-31, substitution was made in no fewer than 255 cases, and with regard to variable X-15 in 6 cases. Few other substitutions were made. The substitutions were performed in order to facilitate the multiple regression analysis. For the regressands, it is also shown in Table 33 how the substitutions took place, but in the regression analyses the unavailable values were excluded, whereby the number of observations varied from one regressand to another (Tables 35 and 36).

Table 34.

Mean values and standard deviations (SD) of regressors and regressands for the follow-up and post mortem series.

Variable	Follow-up series $n_{max} = 267$		Post mortem series $n_{max} = 67$	
	Mean value	SD	Mean value	SD
X-1	1.47	0.50	1.33	0.47
X-2	46.60	13.51	62.66	15.62
X-3	0.76	0.43	0.09	0.29
X-4	0.04	0.20	0.40	0.49
X-5	0.11	0.31	0.03	0.17
X-6	0.09	0.29	0.48	0.50
X-7	32.26	20.08	47.94	23.18
X-8	12.03	0.79	12.40	1.13
X-9	0.48	0.50	0.04	0.21
X-10	0.03	0.17	0.01	0.12
X-11	0.44	0.50	0.70	0.46
X-12	0.04	0.20	0.21	0.41
X-13	0.02	0.15	0.03	0.17
X-14	0.10	0.33	0.24	0.50
X-15	52.50	35.55	28.96	38.38
X-16	4.22	25.99	18.13	40.66
X-17	15.95	18.14	5.73	11.76
X-18	7.42	7.53	15.63	19.14
X-19	0.04	0.61	0.00	0.00
X-20	0.10	0.98	0.42	1.91
X-21	30.08	20.01	46.43	24.33
X-22	0.59	0.38	0.71	0.20
X-23	0.83	0.38	0.52	0.50
X-24	0.01	0.12	0.00	0.00
X-25	0.16	0.36	0.48	0.50
X-26	2.61	1.60	3.73	7.83
X-28	2.10	0.65 n = 125	–	–
X-29	55.51	63.28 n = 69	–	–

TABLE 34 *continued*

Variable	Follow-up series $n_{max} = 267$		Post mortem series $n_{max} = 67$	
	Mean value	SD	Mean value	SD
X-30	0.46	0.50 n = 221	–	–
X-31	4.51	15.28 n = 221	–	–
X-32	0.03	0.18	–	–
X-33	0.13	0.34	–	–
X-34	0.06	0.32	–	–
X-35	0.07	0.29	–	–
X-36	0.06	0.25 n = 252	–	–
X-37	–	–	2.10	1.00
X-38	–	–	2.87	1.19
X-39	–	–	2.57	0.86
X-40	–	–	2.78	0.78
X-41	–	–	2.30	1.07
X-42	–	–	3.21	1.15
X-43	–	–	2.63	0.78
X-44	–	–	2.79	0.86
X-45	–	–	1.10	0.68
X-46	–	–	1.79	1.12
X-47	–	–	1.75	0.89
X-48	–	–	1.64	1.00
X-49	–	–	1.09	0.67
X-50	–	–	2.19	1.16
X-51	–	–	1.54	0.84
X-52	–	–	1.66	1.02
X-53	–	–	1.66	0.95
X-54	–	–	2.64	1.10
X-55	–	–	2.48	0.84
X-56	–	–	2.54	0.88
X-57	–	–	1.75	0.94
X-58	–	–	2.87	1.03
X-59	–	–	2.40	0.82
X-60	–	–	2.57	0.87
X-61	13.75	8.25	–	–
X-62	–	–	10.02	35.02

In Table 34 the follow-up and post mortem series are described by means of mean values and standard deviations for the variables used. The follow-up and post mortem series are treated separately. In the post mortem series, with a few exceptions, data for the postintubation course was lacking, and since the two series consisted of completely different regressands they had to be analysed separately. The difference in the mean duration of intubation between the follow-up and the post mortem series is associated with the fact that in the latter series the patients were often moribund and in these cases it was chosen to allow the endotracheal tube to remain *in situ* instead of performing secondary

tracheostomy. It is worthy of note that in no case was prolonged endotracheal intubation the cause of death. With regard to the regressands, it can be seen in Table 34 that the standard deviation (SD) was considerable. This holds, for example, for X-29, which is also evident in Fig. 10, and for the variables X-37—X-60 in the post mortem series.

Table 35.

Correlation between certain dependent variables and other recorded variables. The table shows the number of adult patients for whom values were recorded for the various regressands. Level of significance marked with asterisks (cf. Statistical Methods).

	X-28 Grade of acute postintubation damage n = 125	X-29 Duration of healing time of acute postintubation damage in the larynx n = 69	X-30 Vocal disturbances > 1 week after extubation n = 221	X-32 Pathological changes in the larynx necessitating surgical treatment n = 267	X-36 Tracheal stenosis at follow-up n = 252
X-1	−0.02	−0.00	0.01	0.11	−0.01
X-2	−0.14	−0.18	0.09	−0.07	0.10
X-3	−0.15	−0.16	−0.13	−0.14	−0.09
X-4	−0.09	−0.09	−0.06	0.07	0.03
X-5	0.33***	0.20	0.18*	0.14	−0.04
X-6	−0.07	0.05	0.03	0.01	0.16*
X-7	0.27**	0.07	0.13	0.01	0.12
X-8	0.04	0.17	−0.05	0.07	−0.05
X-9	0.05	−0.05	−0.28***	−0.10	−0.04
X-10	0.01	−0.07	0.08	0.10	−0.05
X-11	−0.19	−0.05	0.23**	0.11	0.02
X-12	0.24**	0.18	0.04	0.07	−0.06
X-13	0.04	−0.11	0.01	0.11	0.17*
X-14	0.12	0.01	0.16*	0.07	0.17*
X-15	−0.20*	−0.27*	−0.11	−0.15	−0.04
X-16	−0.02	−0.08	−0.02	−0.03	0.11
X-17	−0.07	−0.23*	0.11	−0.10	−0.07
X-18	−0.18	−0.10	0.04	−0.05	0.16*
X-21	0.19*	−0.01	0.09	−0.03	0.13
X-22	−0.01	−0.08	0.09	0.07	0.12
X-23	−0.15	0.18	–	−0.03	−0.43***
X-24	0.25**	0.24*	–	0.15	−0.03
X-25	0.04	−0.26*	–	−0.02	0.46***
X-26	0.01	−0.07	–	−0.02	0.08
X-27	−0.02	–	−0.03	−0.02	0.41***
X-28	–	0.43**	–	–	−0.01
X-29	–	–	–	–	−0.06
X-30	0.30**	0.31*	–	–	−0.15*
X-31	0.19	0.29*	0.33***	0.11	0.01
X-32	0.18	0.35**	0.20**	–	0.03
X-33	0.09	−0.18	0.17*	−0.02	0.07
X-34	−0.03	0.04	0.15	−0.04	0.10
X-35	0.10	0.61***	0.04	0.17*	0.17*

1. *Simple correlation analysis*

Table 35 shows the relationship between different independent variables and the most important dependent variables (the regressands), recorded at the follow-up examination.

As can be seen in Table 35, there were many significant coefficients of correlation. Of especial interest is the correlation found between healing time and grade of damage as recorded in the acute stage ($r = 0.43$). The finding of a mutual correlation between the variables which were recorded at the follow-up examination is hardly surprising. In the following, therefore, the comments will be limited to the relationship between those variables designated as regressors and those designated as regressands in Table 33.

Of the variables which were recorded before extubation, and also "tracheostomy variables", a long duration of endotracheal intubation, tracheostomy performed because of respiratory obstruction and Magill tubes resulted in a higher *grade of acute postintubation damange*, and this also held for patients intubated for the reason of drug poisoning.

With regard to *duration of healing time of acute postintubation damange in the larynx*, it was observed that a higher dose of muscle relaxants and sedatives during the period of intubation resulted in a significantly shorter healing time. Patients subjected to secondary tracheostomy for the reason of expected prolonged artificial ventilation showed a significantly shorter healing time, while those who were tracheostomized for obstruction of the airway showed a longer healing time. The relatively small number of significant correlations may be due to the small number of patients for whom healing time is recorded. With regard to the selection of patients, see p. 28.

Concerning *vocal disturbances > 1 week after extubation*, it was found that these occurred significantly more frequently after the use of Portex tubes, and significantly less frequently with BOC reinforced latex tubes. Otherwise, there was only one almost significant relationship between vocal disturbances and variables recorded before extubation or tracheostomy variables.

No significant relationships were found between *pathological changes in the larynx necessitating surgical treatment* and variables which were recorded before extubation, or tracheostomy variables.

Tracheal stenosis found at follow-up occurred in a significantly higher frequency among patients tracheostomized for the reason of expected prolonged artificial ventilation than among those subjected to prolonged endotracheal intubation alone. Tracheal stenosis observed at the follow-up examination was also more frequent among patients who had been tracheostomized previously—in these patients, stenosis had probably been present before the intubation. Other relationships were considerably weaker, but it is worthy of mention that patients who had had more than one endotracheal tube exhibited a higher frequency of stenosis.

To summarize, it can be said that between, on the one hand, the variables which had been recorded after extubation (the regressands), and on the other

hand those variables which had been recorded before extubation and also tracheostomy variables (the regressors), some correlations were found but these were weak—but nevertheless significant.

2. *Multiple regression analysis*

In view of the results of the simple correlation analysis it was considered important to determine whether the total effect of the regressors had a large explanatory value in relation to the regressands. This study was performed by means of a multiple regression analysis, the results of which for the *follow-up series* are presented in Table 36. Included as regressors (independent variables), were variables recorded before extubation and also tracheostomy variables (X-1—X-27).

Table 36.

Regression coefficients significantly different from 0 and coefficients of determination (R^2) for various dependent variables recorded in the follow-up series. The regressors studied are the same as in Table 33. Cf. Statistical Methods.

Dependent variable		Regressors with significance according to multiple regression analysis		R^2
X-28	Grade of acute post-intubation damage (n = 125)	X-24	Respiratory obstruction after extubation necessitating tracheostomy (* pos.)	0.30
X-29	Duration of healing time of acute post-intubation damage in the larynx (n = 69)	None		0.29
X-30	Vocal disturbances > 1 week after extubation (n = 221)	X-14	More than one tube (* pos.)	0.13
		X-17	Dose of phenoperidine during operation (** pos.)	
X-31	Duration of vocal disturbances (n = 221)	X-15	Dose of tubocurarine during operation (* neg.)	0.05
X-32	Pathological changes in the larynx necessitating surgical treatment (n = 267)	X-1	Sex (* pos.)	0.12
		X-3	Maximal external tube diameter (** pos.)	
X-33	Subjective upper respiratory symptoms at follow-up (n = 264)	X-26	Duration of tracheostomy (* pos.)	0.12
X-34	Vocal disturbances at follow-up (n = 267)	X-2	Age (* pos.)	0.09
		X-25	Tracheostomy for expected prolonged artificial ventilation (* pos.)	
		X-26	Duration of tracheostomy (* neg.)	
X-35	Pathological changes in the larynx at follow-up (n = 267)	X-25	Tracheostomy for expected prolonged artificial ventilation (** pos.)	0.12
X-36	Tracheal stenosis at follow-up (n = 252)	X-25	Tracheostomy for expected prolonged artificial ventilation (*** pos.)	0.33

It can be seen in the last column of Table 36 that the explanatory value, expressed as R^2, was low. At its highest, namely for stenosis, grade of damage and healing time, it was approximately 0.30. This means that approximately 30% of the variation between the different patients with regard to each of these three regressands could be explained by the regressors and that the greater proportion of the variation, i.e. 70%, could not be explained by these factors.

In spite of the low explanatory values, significant regression coefficients were found, which is evident in Table 36. The majority of the significant correlations which are shown in Table 35 did not hold fast at the multiple regression analysis. On the other hand, new significant relationships were found. The strongest correlation was obtained between tracheal stenosis and tracheostomy. The next strongest was obtained between vocal disturbance and the dose of phenoperidine during the period of intubation, and also between

TABLE 37.

Regression coefficients significantly different from 0 and coefficients of determination (R^2) for various dependent variables recorded in the post mortem series. The regressors studied are the same as in Table 33. Cf. Statistical Methods.

Dependent variable	Regressors with significance according to multiple regression analysis	R^2
X-42 Inflammation section 6	X-20 Dose of haloperidol postop. (* neg.)	0.24
X-50 Necrosis section 6	X-5 Drug poisoning (* pos.) X-17 Dose of phenoperidine during operation (* pos.)	0.30
X-58 Ulceration section 6	X-4 General surgery (* pos.) X-5 Drug poisoning (* pos.)	0.36
X-43 Inflammation section 7	X-26 Duration of tracheostomy (* neg.)	0.27
X-51 Necrosis section 7	X-16 Dose of tubocurarine postop. (* pos.) X-26 Duration of tracheostomy (* neg.)	0.39
X-59 Ulceration section 7	X-26 Duration of tracheostomy (* neg.)	0.35
X-44 Inflammation section 8	X-25 Tracheostomy for expected prolonged artificial ventilation (* pos.)	0.23
X-52 Necrosis section 8	X-4 General surgery (* pos.) X-20 Dose of haloperidol postop. (* pos.) X-25 Tracheostomy for expected prolonged artificial ventilation (*** pos.) X-27 Tracheostomy on an earlier occasion (* pos.)	0.45
X-60 Ulceration section 8	X-7 Duration of intubation (* pos.) X-21 Duration of artificial ventilation (* neg.) X-25 Tracheostomy for expected prolonged artificial ventilation (* pos.)	0.37

lesions requiring surgical intervention, on the one hand, and external tube diameter, on the other.

Many of the significances obtained at the 5% level were found to be difficult to explain. In this respect it should be kept in mind that in the analyses which are summarized in the table, about 18×9 regression coefficients were tested, and for that reason alone it might be expected that about 8 significant coefficients at the 5% level would become apparent quite by chance. In fact there were 8 significant coefficients at the 5% level, to which were added 4 coefficients which were more highly significant. It is therefore considered unjustifiable to comment more closely on the almost significant(*) regression coefficients.

In the *post mortem series* a multiple regression analysis was performed with histo-pathological findings as regressands with regard to section 6 infection, section 6 ulceration and section 6 necrosis (Fig. 9; pp. 45 and 46). A similar procedure was carried out with section 7 and section 8. The result of the multiple regression analysis is shown in Table 37.

As can be seen in the last column of Table 37, the explanatory value was low, and the relatively best explanatory value was reached with regard to necrosis in section 8. All of the significant regression coefficients obtained lay at significance level of only 5%, with the exception of X-25 (tracheostomy for expected prolonged artificial ventilation), which gave a significant correlation at a level of $1‰$ for necrosis in section 8. The almost significant coefficients were few and it is therefore considered unjustifiable to comment on them, for the same reason as mentioned above.

B. *Discussion*

The statistical analysis of factors which, before and during the period of intubation, might be considered of importance for different variables characterizing the laryngotracheal status in the postintubation course revealed few simple correlations of interest. The relationship between classified grade of acute damage and healing time was, however, significant at the 1% level. This means that there are certain possibilities at an early stage of predicting the healing course and therewith the risk of late sequelae.

The explanatory values at the multiple regression analysis were low. This probably means that several factors of importance for the occurrence of pathological changes and their healing course were excluded. Interindividual differences in the mucosal resistance and different healing capacities are probably two examples.

With regard to these factors it is conceivable that extremely low haemoglobin or serum protein values should be of importance. These values which had been obtained during the period of hospitalization were therefore checked in patients whose healing course exceeded 1 month and in those with laryngeal

lesions which necessitated surgical therapy. Only in 2 cases was a haemoglobin value below the normal level obtained, however, and the serum protein value lay within normal limits in all patients. In no case was there a prolonged state of shock.

The laryngeal motor activity and movements of the tube during respirator treatment are other factors which are difficult to assess and which were not included in the analysis, since they could not be measured.

The dependent variables which characterized the laryngotracheal status long after the period of intubation might have been influenced by various factors before they were recorded, e.g. vocal strain, infections etc. after the intubation period.

The regressands recorded immediately after extubation, i.e. grade of damage and regressands in the post mortem series, also showed low explanatory values. The classification of the grade of damage was based on macroscopic evaluation of the extent and depth of the lesion which may be a reason why the explanatory value is low.

It cannot be absolutely excluded that factors which did not occur until after the period of hospitalization may have had a high explanatory value for such regressands as healing time and vocal disturbances. There is, however, no support for the assumption that important unrecorded factors occurred during this period; low explanatory values were also found for those dependent variables which were recorded near to the time of extubation.

At the autopsy examination, however, the depth of the lesions could be evaluated fairly precisely, but the explanatory values showed no noteworthy increase here either. There is reason to assume that unrecorded variables influenced the regressands. This assumption must be taken into account when interpreting the significant (at the 1% level) coefficients obtained. There is thus reason to question, in the first place, such correlations which do not appear reasonable. Of those factors which are reasonable and significant at the 1% level, it may be mentioned that a large tube diameter showed a correlation with local laryngeal lesions necessitating surgical therapy (mostly postintubation granulomas) and tracheostomy showed a correlation with deep tracheal lesions and tracheal stenosis.

GENERAL DISCUSSION

This investigation was carried out as a prospective study during the period 1964–1967, and comprised 457 patients. The value of an investigation of this kind was pointed out in 1968 by HARRISON and TONKIN, who remarked on the need for studies to determine the risk of "remote complications" in the larynx.

Only endotracheal intubation for longer than 24 hours was studied, since it is generally considered that intubation for shorter periods does not usually give rise to serious complications.

Problems during the intubation period have been reported by several authors and have consisted of sticky or inspissated secretions in fine-calibre endotracheal tubes. Experiences from the present study indicate that these problems can be overcome to a large extent if the inhaled air or gas mixture is humidified with an ultrasonic nebulizer. With adequate humidification, no cases of insufficient ventilation due to the accumulation of secretions in the endotracheal tube or bronchial tree occurred in the series of patients presented here.

Acute laryngeal damage caused by prolonged endotracheal intubation has been studied clinically by TONKIN and HARRISON (1966) and in post mortem cases by BERGSTRÖM *et al.* (1962) and HEDDEN *et al.* (1969), among others. There has been no standardized clinical classification of the damage, which makes comparisons difficult. Such a classification has been suggested in the present study (see p. 53). It was shown that all patients in the follow-up series of this investigation had some form of damage in the laryngotracheal tract in the initial period following prolonged endotracheal intubation.

The majority had ulceration on the medial sides of the arytenoid cartilages and in the posterior subglottic area of the larynx, but in only a few cases did the ulceration appear to have penetrated so deeply as to damage the cartilage.

At autopsy examination of the present post mortem series the great majority of cases studied showed macroscopic ulceration of the larynx, but in very few cases did this appear to be so deep that the underlying cartilage was exposed. On microscopic examination, however, it was found that about $\frac{1}{3}$ of these patients had ulcers which penetrated the perichondrium on the medial sides of the arytenoid cartilages, and no fewer than $\frac{2}{3}$ had local perichondritis within the same area. Thus there is reason to assume that in cases of damage which was classified clinically as deep ulceration (grade III), the perichondrium was often affected.

Prognostically, this was probably of importance for the development of granulomas, but not, as a rule, for the occurrence of late sequelae. The damage observed in the post mortem series may have been more penetrating than that in the follow-up series due to the fact that the mean duration of intubation

was longer and the mucosal resistance lower in the former than in the latter. A prolonged state of shock with poor circulation, *inter alia*, may have lowered the resistance in the post mortem group.

Acute mucosal lesions in the trachea caused by the cuff of the endotracheal tube were not uncommon, but seldom so pronounced as to produce clinical symptoms. Among the patients subjected to secondary tracheostomy in the follow-up series, a tracheal rupture occurred in one case as a result of pressure necrosis from the prolonged presence of an inflated cuff. In the post mortem series considerably more pronounced mucosal damage was observed in the trachea in the patients subjected to secondary tracheostomy than in those treated by prolonged endotracheal intubation alone. These findings indicate the need for an improved technique for creating a "no leak ventilation" in respirator treatment in order to avoid undue pressure on the tracheal wall. The most interesting and most attractive solution to these problems hitherto has been presented by Lomholt (1967). On the whole it can be said that the frequency of different grades of acute damage as classified clinically, and the post mortem findings are in fairly good agreement.

The healing course for the acute ulcerative lesions was characterized by reversible granuloma formation on the medial sides of the arytenoids. This occurred in about ⅓ of the adult patients, while no granulomas were observed in infants and children. The agreement between the frequency of damage with penetration of the perichondrium on the medial sides of the arytenoid cartilages and the frequency of postintubation granulomas with the same localization makes it probable that these two conditions may be correlated. The postintubation granulomas constituted no clinical problem and in no patient did they give rise to permanent disabilities. The healing times which have been given for granulomas may seem long, but it must be taken into consideration that, with very few exceptions, they produced mild symptoms. What the conditions would have been if the granulomas had been removed surgically at an early stage cannot be stated, since there is no comparative material in this respect. Some authors, however, recommend that the granuloma should not be removed until it has become pedunculated (Epstein and Winston, 1957, Bergström, 1964).

The formation of stenotic fibrous scars in the larynx during the course of healing of acute postintubation lesions was observed in 1 adult and 3 infants and children. These sequelae were serious and necessitated long periods of convalescence. In all 4 patients residual scars were seen at the follow-up examination (after more than 1 year), but in only one case were slight symptoms of laryngeal stenosis still present. In one of these children with subglottic cicatricial stenosis, tracheostomy as an alternative to prolonged endotracheal intubation would have been extremely hazardous in the initial stage, since the patient had undergone colonic transposition for oesophageal atresia and there was a large suppurating wound in the usual tracheostomy region. It is probable that prolonged endotracheal intubation saved this patient's life.

The incidence of stenotic scar tissue in the trachea after secondary tracheostomy was surprisingly high, but is in good agreement with findings in other studies (Kucher *et al.*, 1967, Pearson, 1968, Stoeckel, 1968). The high frequency of tracheal stenosis also agrees well with the high frequency of acute damage to the tracheal cartilage which was found in the post mortem series. Thus there are several indications that a lesion on the perichondrium is related to the development of granulomas and fibrous scars.

The duration of vocal disturbances after prolonged endotracheal intubation was studied in patients who were given this treatment alone, without secondary tracheostomy. Since granulomas often developed in adults, it was not surprising to find that in these patients vocal disturbances with a duration of more than one month were relatively frequent (16%), while no infants or children in this group had such prolonged vocal disturbances. The disturbances were usually mild, and only a few patients complained spontaneously of an altered voice. At the final follow-up examination only about 2% of the patients had vocal disturbances—and these were mild—which could have occurred as a result of prolonged endotracheal intubation. In some of these cases they were caused by internus or transversus paresis and it is uncertain whether this had been present before the period of intubation.

Despite the occurrence of inflammatory reactions, necrosis and ulceration following prolonged endotracheal intubation, and despite the development of granulomas and periods of hoarseness during the healing course, late complications were rare.

Statistical analysis of the correlation between various conceivable causative factors and the laryngeal damage in prolonged endotracheal intubation was performed, but for those independent variables which could be included in the analysis, few significant relationships were found. As mentioned in a previous discussion (see p. 100) there are numerous other possible causes of the damage. The most important probably include laryngeal motor activity and mucosal resistance. These, however, could not be measured and could not, therefore, be evaluated statistically as causative factors.

In an attempt to determine wherein the greatest risk of serious complications lies, a study was made of the circumstances which led to the development of stenotic scars in 4 patients after prolonged endotracheal intubation. In general, it can be said that extreme conditions in one form or another were present in all of these cases. Oversized tubes, extreme pressure on the posterior parts of the larynx (in cases where red rubber tubes were used) and excessive uncontrollable laryngeal motor activity were noted in these patients either separately or in combination. The duration of intubation was not extremely long; in 2 cases it was below average but in 2 cases it exceeded the average. In adults, it was seldom found that tubes with too large an external diameter had been used. In agreement with observations of Tonkin and Harrison (1966), there were signs to indicate that women had often been given larger tubes in relation to the lumen of the larynx than men. Oversized tubes had

more often been used in infants and children than in adults. The margins are narrow where infants are concerned, and *the choice of an adequate tube diameter is one of the most decisive factors for the prevention of late complications.* The size of the lumen at the cricoid level at different ages was reported by BAYEUX (1897). These data are in very good agreement with the clinical experiences in the present study. All 3 children who developed fibrous stenosis in the larynx had a tube with an external diameter which lay at the value given for the diameter at the cricoid level for that age, and in all other children but one the diameter was below this value. BAYEUX's information (see p. 32 in the above mentioned report) on the calibre of the larynx and trachea can be used with advantage as a guide when choosing the tube diameter. The external diameter of the tube should be less than the calibre given for the age in question, but the final choice of diameter must be considered carefully in each individual case.

Particular mention should be made of the fact that no children with subglottic inflammation (pseudocroup) were included in this series, and therefore the risk of prolonged endotracheal intubation for this group of patients cannot be assessed.

Photographic recording of the laryngeal changes was found to be valuable and simplified comparison between the findings at different examinations. Experience has shown that this method should be used to a greater extent in clinical practice.

When choosing between tracheostomy and prolonged endotracheal intubation, the advantages and disadvantages of the two methods must be carefully weighed. The result of this investigation shows that endotracheal intubation, within the time limits which have been usual at this hospital, is relatively free of risk if the technique described under "methods" is used and if the above points with regard to injurious factors are borne in mind.

There has been a tendency for tracheostomy to be delayed as long as possible because of the risk of complications. This is an important and sometimes overlooked reality, although in more recent years it is commonly agreed that if any question arises as to the possible need of tracheostomy, it should be done. It is evident from the literature that not so few deaths are due to delay in performing tracheostomy (NELSON and BOWER, 1957, HEAD, 1961). It would seem more reasonable, however, to give a patient initial artificial ventilation via an endotracheal tube, since essentially normal conditions in the airway are restored if the treatment proves to be unnecessary after a short time. The indications for artificial ventilation can thereby be widened without any appreciable risk of subsequent complications.

CONCLUSIONS

For reduction of the risks in prolonged endotracheal intubation, the following points have been found to be of importance:

1. Continuous bedside supervision of the patient in the department of intensive care by staff who are aware of the risks of this method.
2. Adequate humidification of the inspired air, preferably with an ultrasonic nebulizer.
3. A choice of endotracheal tube which is at least one size smaller than the largest tube which can easily pass through the larynx. In children especial care is required in the choice of tube diameter.
4. Endotracheal tubes which are so shaped that they cause as little trauma as possible to the larynx.
5. Reduction of the laryngeal motor activity, if initially the tube is not well tolerated, by means of sedatives and/or muscle relaxants, especially in adults and older children.
6. Inspection of the larynx during the period of intubation in order to determine whether any initial lesions might mean a risk of permanent sequelae. Deep mucosal lesions which extend along $> \frac{1}{3}$ of the cross-section of the larynx involve a particular risk of the development of stenotic fibrous scars. Lesions with less extension in the anterior commissure of the vocal cords or in the region of the crico-arytenoid joint also involves a risk of sequelae.
7. Inspection of the larynx 1 month after the end of the intubation period.

In the choice between tracheostomy and prolonged endotracheal intubation, the advantages and disadvantages of the two methods must be carefully weighed. If there is a clear indication for prolonged artificial ventilation, this can be started in most cases with a period of endotracheal intubation. This holds especially when the artificial ventilation is required postoperatively, in infancy, on exacerbation of chronic pulmonary diseases, in drug poisoning, in posttraumatic unconsciousness, and in other similar conditions where there is threatening or manifest respiratory insufficiency.

No absolute time limit after which endotracheal intubation should be discontinued can be given on the basis of this study. The intubation times which are generally used, i.e. up to 3 days for adults and adolescents and up to 1 week for infants and children, seem justifiable on the basis of the results obtained. These indicate, however, that the length of a tolerable intubation time must be determined mainly with the guidance of findings on inspection

of the larynx. In making this decision, the risk that acute laryngeal damage might give permanent sequelae must be carefully weighed against the calculated risk of tracheostomy complications. With an adequate operative technique and supervision corresponding to that in prolonged endotracheal intubation, the risks in tracheostomy are considered to be small in the acute stage. Decannulation difficulties in infants and late tracheal stenosis after tracheostomy weigh relatively heavily, however, against the few and relatively mild late complications of prolonged endotracheal intubation, to judge from the present results.

GENERAL SUMMARY

The principal aim of this investigation was to determine, in a prospective study of a clinical series, the extent to which prolonged endotracheal intubation (>24 hours) produced acute or late complications from the respiratory tract, especially the larynx. No such study appears to have been made previously.

A survey of the literature concerning intubation and tracheostomy is made (Chapter I).

The clinical series comprising 457 patients (402 adults and 55 children, 29 of whom were less than 1 year old) is presented (Chapter II).

The indications for prolonged endotracheal intubation in this series are presented and the principles for the treatment are given. Methods used in studying the larynx and trachea are described (Chapter III).

Of the results, the following are especially worthy of note (Chapters IV–VIII):

1. Inspissated secretions in fine-calibre endotracheal tubes, which at the beginning of the investigation period caused difficulties, were well overcome with the introduction of ultrasonic nebulizers.

2. Acute mucosal reactions of various types in the larynx and trachea occurred in all patients after endotracheal intubation, but in most cases these were reversible. In 9 cases they caused airway obstruction after extubation, which necessitated secondary tracheostomy.

3. At post mortem examination of patients who died during or shortly after the period of endotracheal intubation, ulceration which penetrated the medial sides of the arytenoid cartilages was observed in $\frac{1}{3}$, and local perichondritis in the same area in $\frac{2}{3}$.

4. An attempt at classification of acute postintubation damage was made, and this was applied at the primary examination in a later part of the investigation. A statistically significant relationship was found between degree of damage and healing time, which suggests possibilities of predicting, in the acute stage, a healing course with the aid of certain criteria.

5. The healing course of acute postintubation lesions was characterized by the occurrence of reversible granuloma formation on the medial sides of the arytenoid cartilages in about $\frac{1}{3}$ of the adults, but not in any of the children. Vocal disturbances with a duration of more than 1 month occurred frequently in adults (16%) but as a rule they were mild and transient, and in children not subjected to secondary tracheostomy no vocal disturbances of such a duration occurred.

6. Late stationary sequelae after prolonged endotracheal intubation were very few. Subglottic fibrous stenosis occurred in 2 children, however, a partial cicatricial fixation of the left arytenoid cartilage was observed in 1 child and a mild subglottic web developed in 1 adult. The partial cicatricial fixation of the arytenoid cartilage gave rise to mild permanent stenotic symptoms. The other patients became free from symptoms after long periods of convalescence.

7. Tracheal stenosis with a decrease by $>30\%$ of the cross-sectional area of the normal tracheal lumen occurred in about 0.5% of patients subjected to prolonged endotracheal intubation alone. Of those who also underwent secondary tracheostomy, about every third patient developed a stenosis of this extent. A long duration of tracheostomy was not necessary for the occurrence of stenosis.

8. Prolonged endotracheal intubation caused no deaths in this series.

9. The reason for lesions which caused acute obstruction of the airway after the period of intubation, and of which some healed with fibrous laryngeal stenosis, was most often the use of an endotracheal tube with too large an external diameter in relation to the lumen of the larynx. A large tube diameter was found to have a statistically significant relationship with pathological changes (mostly postintubation granuloma) which necessitated surgical therapy in adults. An unfavourable shape of the endotracheal tube and excessive laryngeal motor activity were also important causative factors.

10. The duration of intubation, within the limits which were usual in the present series, was found to have no marked relationship with the postintubation course. The duration allowed is completely dependent upon the magnitude of the traumatizing effect of the tube on the larynx per time unit, and on the resistance of the laryngeal mucosa.

11. A primary condition for reduction of the injurious effects of the endotracheal tube is that its shape should agree with the anatomical shape of the airway. A tube has been designed which fulfils this requirement.

12. Prolonged endotracheal intubation has proved valuable as an alternative to tracheostomy and has been used to advantage when artificial ventilation has been necessary postoperatively, in infancy, on exacerbation of chronic pulmonary diseases, in drug poisoning and in posttraumatic states of unconsciousness, among other conditions with temporary respiratory insufficiency.

STATISTICAL METHODS

Notation

Number of cases: $N = n$

$$\text{Mean: } M = \frac{\Sigma X_i}{n}$$

where X_i denotes the value for the i^{th} case.

Standard deviation:

$$SD = \sqrt{\frac{\Sigma(X_i - M)^2}{n - 1}}$$

Standard error: SE

Correlation analysis. The correlation coefficient, r, of x and y is defined by the expression:

$$r = \frac{\Sigma(x_i - \bar{x})\,(y_i - \bar{y})}{\sqrt{\Sigma(x_i - \bar{x})^2\,\Sigma(y_i - \bar{y})^2}}$$

where $\bar{x}$ and $\bar{y}$ denote the means for the $\bar{x}$ and $\bar{y}$ series respectively.

Significance tests

1. In testing whether the regression coefficients differed from 0, the method described by Cramér (1945) and Hald (1948), was used:

A t-value was produced from the expression: $\frac{b_j}{SEb_j}$

2. In testing whether a correlation coefficient differed from 0, the following ratio was produced:

$$\frac{r}{\sqrt{1 - r^2}}\sqrt{n - 2}$$

which—if the true correlation was zero—was considered to be distributed like Student's t, with n-2 degrees of freedom.

Significance levels

The term "significant" is used in accordance with the following convention. If an observed difference between two means is of such magnitude that the probability, P, of obtaining a difference at least as great as the observed value

is greater than 0.05 (where the null-hypothesis is assumed to hold), then that observed difference is said to be non-significant.

If $0.01 < P < 0.05$, the difference is said to be almost significant and is marked*.

If $0.001 < P < 0.01$, the difference is said to be significant and is marked**.

If $P < 0.001$, the difference is said to be (highly) significant and is marked ***.

Multiple regression analysis used in the present study

For a series of n patients we wish to study the relation between a dependent variable, y, called the regressand, and a set of explanatory variables, $x^{(1)} \ldots x^{(k)}$, called regressors. The regressands are, e.g., variables in the postintubation course. The k regressors $x^{(1)} \cdot x^{(2)} \ldots x^{(k)}$, may be age, sex etc.

In order to study the relation between the y and x variables, a type of equation must first be laid down. Individual numerical values must also be available for each variable. In the present work equations of the following form have been studied:

$$y = b_0 + b_1x^{(1)} + b_2x^{(2)} + \ldots b_kx^{(k)}$$

where b_0, b_1, $b_2 \ldots b_k$ are the coefficients which are to be estimated. In estimating these coefficients the principle of least squares has been applied. This principle means that we seek values of coefficients which are constituted in such a way as to yield the smallest possible sum from the following expression:

$$\Sigma(y_i - b_0 - b_1x_i^{(1)} - b_2x_i^{(2)} \ldots b_kx_i^{(k)})^2$$

If this expression is treated in a purely mathematical fashion, as a maximum –minimum problem we obtain a general solution with the aid of the following $k + 1$ linear equations in the $k + 1$ unknown coefficients:

$$\left\{\begin{array}{l} \Sigma y = b_0 n + b_1\Sigma x^{(1)} + \ldots + b_k\Sigma x^{(k)} \\ \Sigma yx^{(1)} = b_0\Sigma x^{(1)} + b_1\Sigma x^{(1)}x^{(1)} + \ldots + b_k\Sigma x^{(k)}x^{(1)} \\ \Sigma yx^{(2)} = b_0\Sigma x^{(2)} + b_1\Sigma x^{(1)}x^{(2)} + \ldots + b_k\Sigma x^{(k)}x^{(2)} \\ \hline \Sigma yx^{(k)} = b_0\Sigma x^{(k)} + b_1\Sigma x^{(1)}x^{(k)} + \ldots + b_k\Sigma x^{(k)}x^{(k)} \end{array}\right.$$

Here Σy stands for the sum of all individual y values and $\Sigma yx^{(1)}$ the sum of all individual products of $yx^{(1)}$ etc.

The principle of least squares has been described in detail by Cramér (1945) and Hald (1948), who also explain the method of calculating SE for the coefficients.

Predicted value

The y value for an individual (i), predicted with the aid of the regression equation, is defined as:

$$b^0 + b_1x_i^{(1)} + b_2x_i^{(2)} + \ldots + b_kx_i^{(k)}$$

R = Correlation between observed y-value and predicted y-value.

The regression analysis program

In treating the data, as stated above, the following regression analysis program was used: Hodson Thornber. Manual for (B34T, 8 Mar 66) a stepwise regression program. Report 6603. Univ. of Chicago, March 1966 (stencil).

All statistical analyses were performed in collaboration with Associate Professor G. Eklund, Ph. D. at the Department of Statistics, University of Stockholm.

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Carl-Eric Lindholm

COLOUR PLATES

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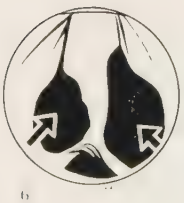
1. Case 209: 41-year old woman with exacerbation of chronic pulmonary disease, intubated with a 10.9 mm external diameter (e.d.), 7.5 mm internal diameter (i.d.) PVC tube for 30 hours. Slight erythema is seen on the medial side of the arytenoids (arrows) and also within the posterior part of the larynx. The reaction was classified as grade I. The photograph was taken on extubation.

2. Case 222: 42-year old man with drug poisoning, intubated with a 10.2 mm (e.d.) PVC tube for 47 hours. Postintubation lesions on the medial sides of the arytenoids (arrows) and within the posterior part of the larynx were classified as grade II. The photograph was taken 24 hours after extubation.

3. Case 265: 63-year old man with postoperative respiratory insufficiency, intubated with a 12.4 mm (e.d.) PVC tube for 72 hours. Postintubation lesions on the medial sides of the arytenoids (arrows) were classified as grade III. The photograph was taken on extubation.

4. Case 226: 57-year old woman with status asthmaticus, intubated with a 11.6 mm (e.d.) PVC tube for 25 hours. A circular postintubation lesion at the cricoid level (arrow) was classified as grade III. The photograph was taken on extubation and illustrates the immediate effect of a tube which is too wide in relation to the lumen of the larynx.

5. Case 318: 30-year old woman with drug poisoning, intubated with a 10.9 mm (e.d.) PVC tube for 61 hours. a) Circular postintubation lesions at the level of the vocal cords (arrow). The lesions were classified as grade III. As in the foregoing case, the tube had been too wide. The photograph was taken on extubation. b) 1 month later the lesions had healed.



6. Case 312: 22-year old man with drug poisoning, intubated with a 12.0 mm (e.d.) Magill red rubber tube for 24 hours. a) Laryngeal status 24 hours after extubation. The lesions were classified as grade III. The tissue reactions on the medial sides of the arytenoids (arrows) were in this case more pronounced. b) 16 days after the intubation period a lesion was still present on the right vocal process. c) 32 days after the intubation period, healing had taken place without sequelae.

7. Case 310: 26-year old woman with drug poisoning, intubated with a 11.6 mm (e.d.) PVC tube for 60 hours. a) Laryngeal status 24 hours after extubation. The postintubation lesions (arrows) were classified as grade II. They were covered by a thin membrane, however, which made assessment more difficult. b) 18 days after the extubation only a minimal lesion remained on the medial side of the left arytenoid. c) 32 days after the intubation period, healing had occurred.

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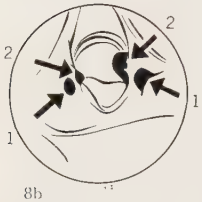

8b

8. Case 309: 27-year old woman with drug poisoning, intubated with a 12.0 mm (e.d.) Magill red rubber tube for 9 hours and then a 10.9 mm (e.d.) PVC tube for 26 hours. a) Laryngeal status 24 hours after extubation. Postintubations lesions (arrows), which were classified as grade III, were noted within about ¾ of the circumference of the larynx at the vocal cord level, and also subglottically. b) 20 days after the intubation period granulomas had formed bilaterally on the medial sides of the vocal processes (arrows 1) and within the posterior lateral circumference of the cricoid ring (arrows 2). c) 34 days after the intubation period, pronounced regression of the granulomas had taken place. d) 64 days after the intubation period the lesions had healed without sequelae.

9a

9b

9. Case 249: 24-year old man with drug poisoning, intubated with a 13.1 mm (e.d.) PVC tube for 35 hours.
a) Laryngeal status on extubation. (The photograph is of poor quality due to damage to the optical equipment). The postintubation lesions on the medial sides of the arytenoids (arrows) were classified as grade III.
b) 44 days after the intubation period, broad-based granulomas had formed (arrows).
c) 55 days after the intubation period some regression of the granulomas had taken place.
d) 81 days after the intubation period the left granuloma had regressed completely, and the right had decreased further in size.
e) 4 months after the intubation period the left granuloma had also disappeared.

10a

10. Case 241: 25-year old woman with drug poisoning, intubated with a 12.4 mm (e.d.) PVC tube for 36 hours. The postintubation lesions on the medial sides of the vocal processes were classified initially as grade III.
a) 46 days after the intubation period, granulomas had formed on the vocal processes (arrows). (The photograph is of poor quality due to damage to the optical equipment).
b) 64 days after the intubation period, spontaneous regression had taken place, especially on the left side.
c) 4 months after the intubation period the granulomas had regressed totally. A submucous haemorrhage in the anterior part of the left vocal cord was observed. Three days before the photograph was taken the patient had suddenly become hoarse on vocal effort. At a subsequent follow-up examination the vocal cord had returned to normal.

8a
8b
8c
8d
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9e
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10c

11b

11. Case 189: 70-year old woman with myasthenia gravis, intubated with a 11.6 mm (e.d.) PVC tube for 3 days. a) and b) Laryngeal status on extubation. The postintubation lesions were classified as grade II and were localized on the medial sides of the arytenoids (arrows 1) and within the inner posterior part of the cricoid ring (arrow 2). c) Only 9 days after the extubation the lesions on the medial sides of the arytenoids had almost healed. The motor activity of the vocal cord in this patient was negligible.

12a

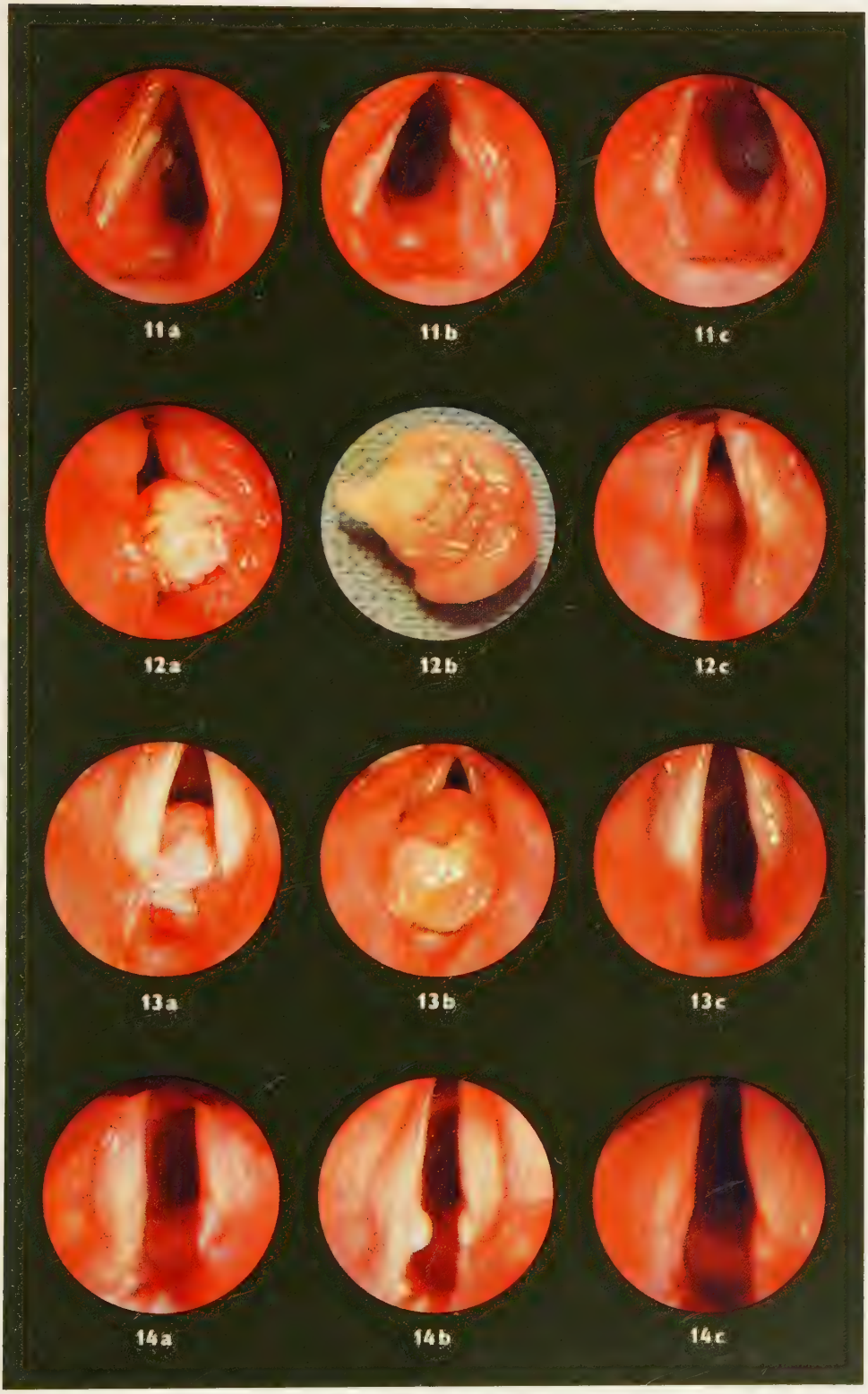
12. Case 305: 37-year old man with status asthmaticus, intubated with a 13.1 mm (e.d.) PVC tube for 48 hours. The initial postintubation lesions were classified as grade III. a) A granuloma (arrow) had gradually developed on the right vocal process, and began to give respiratory difficulties. b) The still broad-based granuloma was extirpated 5½ months after the intubation period. c) 40 days after the removal of the granuloma the mucosa was completely epithelialized.

13a

13. 37-year old woman who, after a traffic accident, was intubated with a 12.0 mm (e.d.) Magill red rubber tube for 1 hour. After 3 months she began to have periods of slight hoarseness, and a small postintubation granuloma was observed. This grew rapidly. a) and b) The granuloma (arrow) had become pedunculated, and 5 months after the intubation period it gave respiratory difficulty and was therefore removed. c) Healing took place within 1 month after removal of the granuloma.

14b

14. Case 256: 28-year old man with drug poisoning, intubated with a 12.0 mm (e.d.) Magill red rubber tube for 10 hours and with a 13.1 mm (e.d.) PVC tube for 16 hours. The initial postintubation lesions were classified as grade II. a) 32 days after the intubation period the lesions appeared to be healed. b) A mucosal cyst (arrow) developed, however, on the left vocal process and was still present 10 months after the intubation period, when it was removed.
c) After a further 40 days the mucosa was well epithelialized at the previous localization of the cyst.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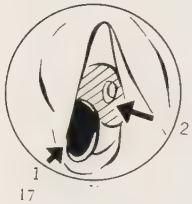
14c

15a

15. Case 287: 23-year old woman with drug poisoning, intubated with a 12.0 mm (e.d.) Magill red rubber tube for 88 hours. The initial postintubation lesions were classified as grade IV. a) 44 days after the intubation period, a granuloma was seen 5 mm below the plane of the vocal cord within the posterior part of the subglottic area (arrow). b) 56 days after the intubation period the granuloma had begun to change to a fibrous scar. c) 4 months after the intubation period a fibrous web had developed. d) 6 months after the intubation period the condition was unchanged and the scar tissue was extirpated. e) 4 months after the removal of the scar tissue, only a slight elevation well coated with mucosa was seen at the site of the fibrous scar.

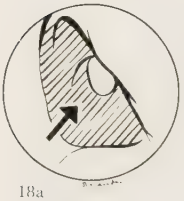
16

16. Case 323: 36-year old man with drug poisoning, intubated with the anatomically shaped PVC endotracheal tube designed by the author (see p. 64). A 10.9 mm (e.d.) tube was used for 45 hours, and the photograph shows ulcerations (arrows) on the medial sides of the vocal processes, but intact mucosa within the posterior circumference of the larynx. (The vocal cords are concealed by part of the instrument).



17

17. Case 190: 44-year old woman submitted to transventricular dilatation of the mitral ostium and intubated postoperatively with a 12.4 mm (e.d.) PVC tube for 28 hours, after which she was tracheostomized and had a cuffed tracheal cannula for 5 days. The photograph was taken 1 year and 2 months after the acute stage and shows a subglottic left-sided postintubation granuloma (arrow 1) and also a pronounced tracheal stenosis (arrow 2), which was located at the site of the cuff of the tracheal cannula (Table 26).

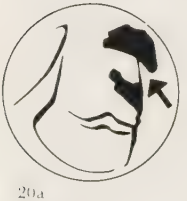


18a

18. Case 209: 41-year old woman with exacerbation of chronic pulmonary disease, intubated for 30 hours (see Plate I:1) and then tracheostomized and ventilated with a high insufflation pressure via a cuffed tracheal cannula for 18 days. The cannula was removed after a further 14 days. The patient began to have progressive stridor. a) 38 days after the decannulation a pronounced tracheal stenosis (arrow) had developed, resulting in retracheostomy and dilatation treatment with a PVC cannula during 6 months. b) 3 months after the dilatation treatment the mucosa of the stenotic part had become epithelialized and the trachea was of adequate width. The distance from the end of the optical instrument to the stricture was not the same in 18 a and 18 b. The diameter at the stricture was, however, measured on frontal X-rays on the two occasions illustrated here, and was found to be 5 and 11 mm, respectively.

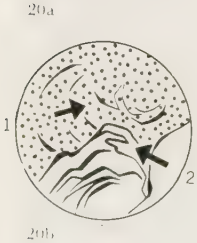
19

19. Case 232: 70-year old man submitted to prostatectomy and intubated postoperatively with a 13.1 mm (e.d.) PVC tube for 47 hours. The patient was then tracheostomized and had a tracheal cannula for 2 days. The photograph was taken 1 year later and shows the development of stenosis from the sides at the level of the tracheostoma (arrow 1). Multiple congenital osteochondroma were also seen in the tracheal mucosa (arrow 2).

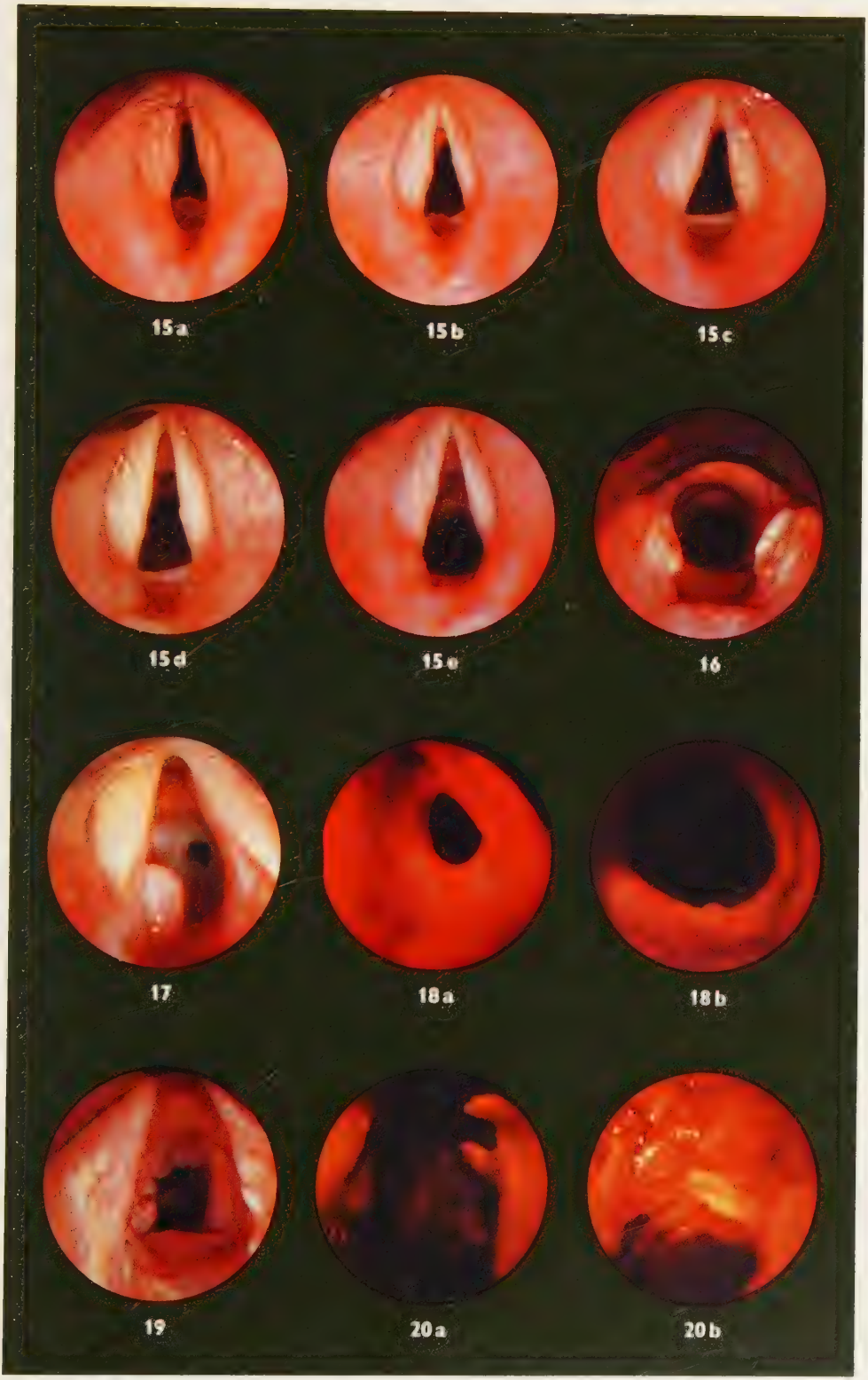


20a

20. Case 180: 41-year old woman with drug poisoning (meprobamate and barbiturate), and initially in a very poor condition, with a state of shock and oliguria. She was ventilated via an endotracheal tube for a few days and then tracheostomized and treated with a respirator via a cuffed tracheal cannula for another 21 days. After this time the patient suddenly developed a pronounced subcutaneous and mediastinal emphysema, which was due to a tracheal rupture at the level of the cuff of the tracheal cannula. a) The ruptured cartilaginous skeleton (arrow) below the tracheostoma seen through the bronchoscope. b) The lower ventral section of the ruptured tracheal wall. The praetracheal soft tissues are exposed (arrow 1). Eroded tracheal cartilage (arrow 2). The patient was then treated with a longer tube, the cuff of which could be placed distal to the erosion, but she died 3 days later.



20b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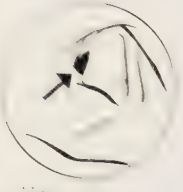
21. 1-month old boy with sepsis, intubated with a 3.7 mm (e.d.) PVC tube for 35 hours. On extubation after prolonged intubation of infants, a laryngeal condition as illustrated in this photograph is usually seen (arrow 1, vocal cord; arrow 2, arytenoid region). The reaction was classified as grade I. Later the patient died of his primary disease.



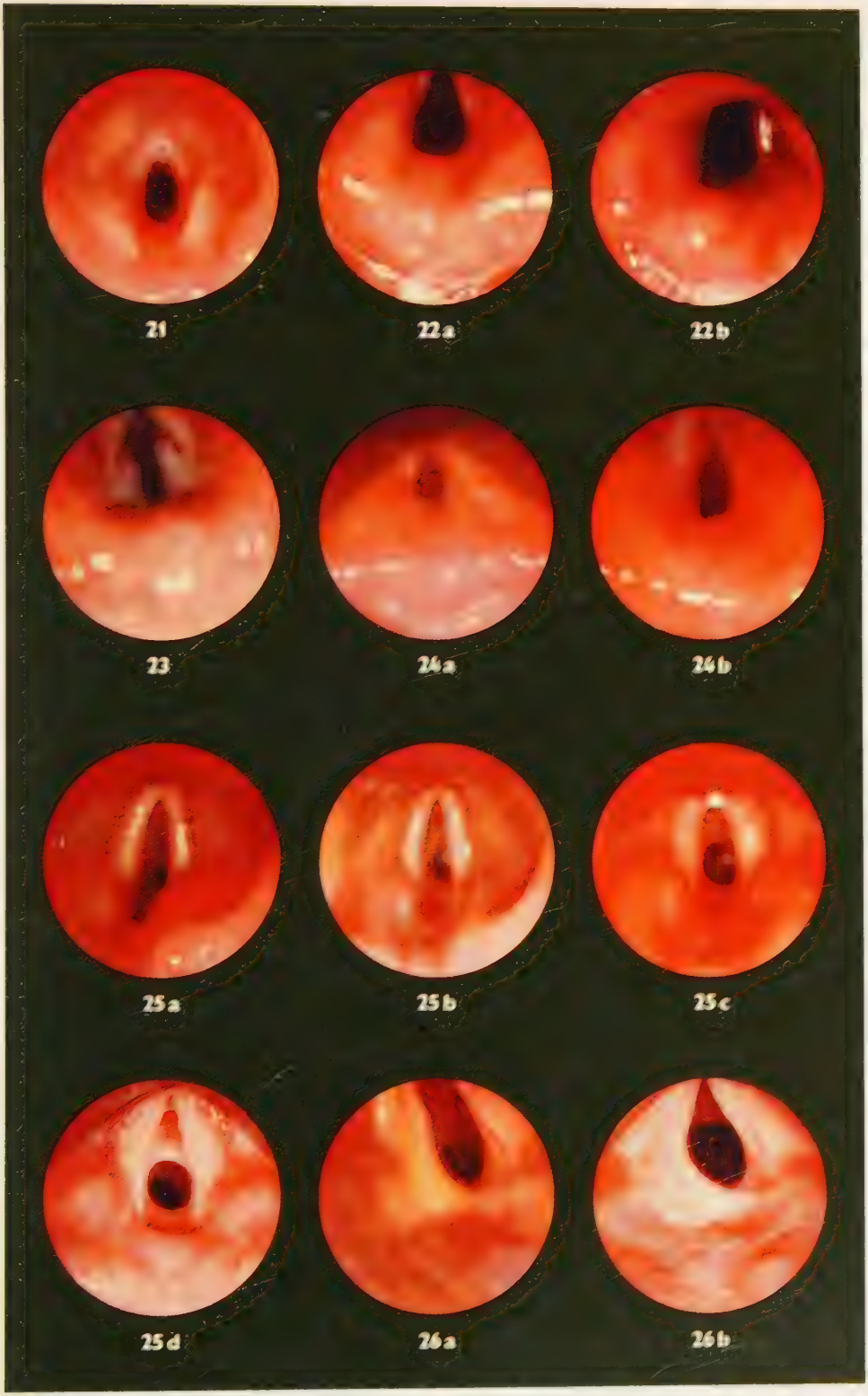
22. Case C 23: 1½-month old boy with transposition of the great vessels, submitted to a Blalock-Henlon operation and intubated postoperatively with a 5.1 mm (e.d.) PVC tube for 21 days. a) and b) The photographs were taken 4 days after extubation, and show moderate oedema in the arytenoid region and a minor mucosal lesion on the posterior part of the left vocal cord (arrow) but a free airway. The lesion was classified as grade II and regressed completely within a further few days.

23. Case C 24: 2-week old boy submitted to operation for transposition of the great vessels and intubated postoperatively with a 5.5 mm (e.d.) reinforced latex tube for 84 hours. The photograph was taken 7 days after extubation and shows moderate swelling bilaterally in the subglottic area (arrows). The reaction was classified as grade I and regressed completely within a further few days.

24. Case C 36: 4-month old boy with congenital heart disease and pneumonia, intubated with a 5.9 mm (e.d.) PVC tube for 3 days and with a 5.1 mm (e.d.) PVC tube for 5½ days. After this period tracheostomy was performed. a) The photograph was taken on extubation and shows ulceration on the medial side of the right arytenoid region (arrow). The lesion was classified as grade II. b) On examination 49 days after the intubation the lesion was healed. The patient died 3 months later (specimen, Fig. 18), however, of his primary disease, having had respirator treatment for the whole time except for short periods.

25. Case C 20: 1½-year old boy subjected to colonic transposition for oesophageal atresia and intubated postoperatively with a 7.0 mm (e.d.) reinforced latex tube for 26 hours. 33 hours after the extubation the patient was reintubated because of stridor caused by subglottic swelling. A 5.1 mm (e.d.) PVC tube was first used for 44 hours, and then a 6.6 mm (e.d.) PVC tube for 3 days. On extubation a subglottic circular mucosal necrotic lesion was noted at the level of the cricoid ring, and this lesion was classified as grade IV. Secondary tracheostomy was performed.
a) 31 days after the intubation period a pronounced fibrous subglottic stenosis (arrow) had developed.
b) 71 days after the intubation period, bouginage had resulted in considerable widening of the stenotic area.
c) 4½ months after the intubation period further regression of the stenosis had taken place and the cannula was removed.
d) 1 year and 5 months after the intubation period some stenosis was still seen but the patient had no symptoms.

26. Case C 3: 8-year old boy with a skull injury and general convulsions, intubated with a 9.0 mm (e.d.) Magill red rubber tube for 36 hours. On the medial sides of the arytenoids and within the interarytenoid area, deep ulcerations occurred as a result of excessive laryngeal activity, and these were classified initially as grade IV. Tracheostomy was performed and the tracheal cannula was removed 4 days later.
a) Laryngeal status 1 year and 3 months after the intubation period. A fibrous scar partly fixed the left arytenoid region.
b) 2 years and 8 months after the intubation period, full abduction of the left vocal cord was still prevented by the scar formation (arrow), and the boy had slight stridor on physical effort.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